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- Applicant: TAKEDA CHEMICAL INDUSTRIES, LTD. 3-6, Doshomachl 2-chome Chuo-ku Osaka 541(JP)
- (2) Inventor: Goto, Giichi
 6-11, Kofudai 5-chome, Toyono-cho
 Toyono-gun, Osaka, 563-01(JP)
 Inventor: Ohkawa, Shigenori
 45-20, Makamicho 6-chome
 Takatsuki, Osaka, 569(JP)
 Inventor: Fukumoto, Shoji
 21-72, Takenodai 1-chome, Nishi-ku
 Kobe, Hyogo, 673(JP)
- Representative: Laredo, Jack Joseph et al Elkington and Fife Beacon House 113 Kingsway London, WC2B 6PP(GB)
- (a) Nitrosothiol derivatives, their production and use.
- Novel nitrosothiol derivatives of the formula:

$$X_1 - \frac{X_2}{N} > CH - \frac{K_1}{C} - SNO$$

wherein R^1 and R^2 are independently a hydrogen atom or a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is a hydrogen atom, an acyl group, a lower alkoxy group or a hydrocarbon residue which may be substituted; X^2 is an acyl group or a carboxyl group which may be esterilied or which may form an amide; with a proviso that when X^2 is a carboxyl group X^1 is not a hydrogen atom or acetyl group and that when both R^1 and R^2 are hydrogen atoms X^1 is not an acetyl group or γ -glutamyl group, and salts thereof, show excellent hypotensive action, anti-arrhythmic action, anti-anginal action, cardiotonic action or coronary vasodilation, thus being useful as therapeutic or prophylactic agents for the cardiovascular diseases such as hypertension and angina pectoris.

NITROSOTHIOL DERIVATIVES, THEIR PRODUCTION AND USE

BACKGROUND OF THE INVENTION

This invention relates to novel S-nitrosothiol derivatives which are useful as medicines, especially as therapeutics for the cardiovascular diseases such as hypertension and angina pectoris.

Along with aging of society, hypertension and heart diseases have become matters of primary concern, and various cardiovascular medicines have been developed for the treatment of such diseases. There are prior art documents disclosing the production of some nitro-compounds and nitrites among the medicines [Journal of Pharmacy and Pharmacology, 31, 801 (1979)].

In the social circumstances described above, more reasonable agents are being required to be developed in the field of cardiovascular drugs, particularly antihypertensives and therapeutics for angina pectoris. However, satisfactory compounds have not yet been found. There have been no report so far for the application of S-nitrosothiol derivatives as therapeutics for angina pectoris.

DETAILED DESCRIPTION

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As a result of the research to find out useful compounds as therapeutics for cardiovascular diseases, especially as anti-hypertensives and therapeutics for angina pectoris, the present inventors have found that the compounds represented by the formula (1):

$$\frac{X^{1} - \frac{R^{3}}{N}}{X^{2}} > CH - \frac{R^{1}}{C} - SNO$$
 (1)

wherein R^1 and R^2 represent respectively a hydrogen atom or a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is a hydrogen atom, an acyl group, a lower alkoxy group or a hydrocarbon residue which may be substituted; X^2 is an acyl group or a carboxyl group which may be esterified or form an amide; and when X^2 is a carboxyl group X^1 is not a hydrogen atom or acetyl group, and when both R^1 and R^2 are hydrogen atoms X^1 is not acetyl group or gamma-glutamyl group, and the salts thereof are excellent in alleviation of the cardiovascular diseases, and have completed the present invention.

The "hydrocarbon residues" in the above-mentioned "hydrocarbon residues which may be substituted" in the formula (I) include, chain-, cyclic-, saturated-, and unsaturated-hydrocarbon residues, and various combinations thereof. Chain-hydrocarbon residues include straight chain and branched alkyl groups each having 1 to 6 carbon atoms (e.g. methyl, ethyl, n-propyl, i-propyl, i-butyl, i-butyl, tert-butyl, n-pentyl, n-hexyl).

Chain unsaturated hydrocarbon residues include straight chain and branched C_{2-4} -alkenyl (e.g. vinyl, allyl, 2-butenyl), and C_{2-4} -alkynyl (e.g. propargyl, 2-butynyl).

Cyclic saturated hydrocarbon residues include monocyclic cycloalkyl having 3 to 7 carbon atoms (e.g. cyclobutyl, cyclopentyl, cyclohexyl), and bridged cyclic saturated hydrocarbon residues having 8 to 14 carbon atoms (e.g. bicyclo[3,2,1]oct-2-yl, bicyclo[3,3,1]nonan-2-yl). Cyclic unsaturated hydrocarbon residues include phenyl and naphthyl groups.

R1 and R2 may be bound with each other to form a ring of -(CH2)n- wherein n is an integer of 2 to 6.

Substituents for these hydrocarbon residues include halogen atoms (e.g. chlorine, bromine, and iodine atoms), nitro, nitrile, hydroxyl, carboxyl, C_{1-4} -alkoxy (e.g. methyloxy, ethyloxy, propyloxy, butyloxy, isopropyloxy), C_{1-4} -alkylthio (e.g. methylthio, ethylthio, propylthio, isopropylthio, butylthio), amino, mono- or di- C_{1-4} -alkyl substituted amino (e.g. methylamino, ethylamino, propylamino, dimethylamino, diethylamino), mono- or di-aralkyl substituted amino (e.g. benzylamino, 2-hydroxyphenylmethylamino), mono-or di-pyridyl-carbonyl substituted amino (e.g. 3-pyridylcarbonylamino), C_{1-4} alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isobutoxycarbonyl), hydroxycarbonyl, C_{1-6} -alkylcarbonyl (e.g. methylcarbonyl, cyclo C_{3-6} -alkylcarbonyl (e.g. cyclopentylcarbonyl, ethylcarbamoyl, mono- or di- C_{1-4} -alkyl-substituted carbamoyl (e.g. methylcarbamoyl, ethylcarbamoyl,

propylcarbamoyl, butylcarbamoyl, diethylcarbamoyl, dibutylcarbamoyl), and phenyl, phenoxy, benzoyl, phenoxycarbonyl, phenyl C_{1-4} -alkylcarbamoyl (e.g. benzylcarbamoyl, phenethylcarbamoyl) and phenylcarbamoyl which may have 1 to 4 substituents [substituents in the respective phenyl group include C_{1-4} -alkyl group (e.g. methyl, ethyl, propyl, butyl, isopropyl), halogen atom (e.g. chlorine, bromine, iodine atoms), hydroxyl, benzyloxy, amino, mono- or di- C_{1-4} -alkyl-substituted amino (e.g. methylamino, ethylamino, propylamino, dimethylamino, diethylamino, methylethylamino), nitro, C_{1-4} -alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl)].

The appropriate number of the substitutents in each of these hydrocarbon residues is 1 to 3.

Acyl groups represented by R³, X¹, and X² include carboxylic acyl, carbamic acyl, sulfonic acyl, and substituted oxycarboxylic acyl groups, all of which may be substituted. When an acyl group is substituted, the substituents include those for the hydrocarbon residues described above.

Carboxylic acyl groups include C_{1-6} alkylcarbonyl such as formyl, acetyl, propionyl, butyryl, valeryl, hexanoyl, isobutyryl, and isovaleryl (which may be substituted, for example, with amino, 3-carbamoyl-1,4dihydropyridin-1-yl, 3-carbamoyl-1-pyridyl, or phenoxy; substituted C1-5-alkylcarbonyl groups are exemplified by phenoxyacetyl, 4-aminobutyryl, aminomethylcarbonyl, 2-(3-carbamoyl-1,4-dihydropyridin-1-yl)ethylcarbamoyl, and 2-(3-carbamoylpyridin-1-yl)ethylcarbamoyl), C3-8cycloalkylcarbonyl such as cyclopentylcarbonyl and cyclohexylcarbonyl, C_{3-8} cycloalkyl- C_{1-6} alkylcarbonyl such as cyclopentylacetyl, C_{2-6} -salkenyi or alkynylcarbonyl such as acryloyl, crotonoyl, 2-pentenoyl, 4-pentynoyl, 2-hexenoyl, 3-hexenoyl, and 2,4-hexadienoyl, aryl carbonyl such as benzoyl, and naphthoyl, pyridylcarbonyl such as nicotinoyl, and 20 dihydropyridylcarbonyl [which may be substituted, for example, with C1-4alkyl (e.g. methyl, ethyl, propyl, butyl), benzyl, methoxycarbonyl, 3-nitrophenyl, nitro, or 2-trifluorophenyl; substituted dihydropyridylcarbonyl groups are exemplified by N-C₁₋₄alkyl-1,4-dihydropyridine-3-carbonyl (e.g. N-methyl-1,4-dihydropyridine-3carbonyl, N-ethyl-1,4-dihydropyridine-3-carbonyl, N-butyl-1,4-dihydropyridine-3-carbonyl), N-benzyl-1,4dihydropyridine-3-carbonyl, 2,6-dimethyl-5-methoxycarbonyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-ylcarbonyl, and 2,6-dimethyl-5-nitro-4-(2-trifluorophenyl-1,4-dihydropyridine-3-ylcarbonyl), pyridiniumcarbonyl (in which the nitrogen in the pyridine ring is substituted, for example with C1-4alkyl (e.g. methyl, ethyl), or benzyl, and exemplified by C_{1-4} alkylpyridinium-3-carbonyl (e.g. methylpyridinium-3-carbonyl, ethylpyridinium-3-carbonyl, propylpyridinium-3-carbonyl), and benzylpyridinium-3-carbonyl).

Carbamic acyl groups include carbamoyl, mono- or di- substituted carbamoyl groups. The mono- and di- substituted carbamoyl groups include mono- and di- C_{1-4} aikylcarbamoyl such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, butylcarbamoyl, dimethylcarbamoyl, diethylcarbamoyl, and dipropylcarbamoyl, mono- and di- C_{3-6} -alkenyl- and alkynylcarbamoyl such as allylcarbamoyl, 3-butenylcarbamoyl, 4-pentenylcarbamoyl, and diallylcarbamoyl, mono- and di-aromatic group carbamoyl such as phenylcarbamoyl, naphthylcarbamoyl, and diphenylcarbamoyl.

Sulfonic acyl groups include inorganic sulfonyl such as sodiumsulfonyl, C_{1-6} alkylsulfonyl such as methylsulfonyl, ethylsulfonyl, propylsulfonyl, and butylsulfonyl, C_{2-6} alkenyl- or alkynylsulfonyl such as allylsulfonyl, and 2-methyl-2-propenesulfonyl, and aromatic sulfonyl such as phenylsulfonyl, p-methylphenylsulfonyl, and naphthalenesulfonyl.

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Substituted oxycarboxylic acyl groups include C_{1-6} alkyloxycarbonyl which may be substituted with halogen (e.g. chlorine, bromine, iodine), cyano, benzyloxy, phenoxy, di C_{1-3} alkylamino (e.g. dimethylamino, diethylamino, dipropylamino), C_{1-4} alkyloxy (e.g. methyloxy, ethyloxy, butyloxy, t-butyloxy), C_{1-3} alkylthio (e.g. methylthio, ethylthio, propylthio), 4-(3-nitrophenyl)-2,6-dimethyl-3-methoxycarbonyl-1,4-dihydropyridin-5-ylcarbonylamino or dihydropyridylcarbonylamino (methyloxycarbonyl, ethyloxycarbonyl, n-propyloxycarbonyl, i-propyloxycarbonyl, n-butyloxycarbonyl, sec-butyloxycarbonyl, t-butyloxycarbonyl, n-hexyloxycarbonyl, 2-fluoroethyloxycarbonyl, 2-chloroethyloxycarbonyl, 2,2,2-trichloroethyloxycarbonyl, and 3-methyl-1,4-dihydropyridin-1-ylcarbonylaminomethyloxycarbonyl), C_{3-8} cycloalkyloxycarbonyl (which may be substituted, for example, with halogen such as chlorine, bromine, and iodine) such as cyclopentylmethyloxycarbonyl, C_{2-7} alkenyl- or alkynyloxycarbonyl such as allyloxycarbonyl, crotyloxycarbonyl, and 2-pentene-1-oxycarbonyl, aromatic or aromatic-aliphatic oxycarbonyl (which may be substituted, for example, with halogen such as chlorine, bromine and iodine, or nitro) such as phenyloxycarbonyl, benzyloxycarbonyl, and phenethyloxycarbonyl, and quinuclidinyl.

Lower alkoxy groups represented by X¹ include those represented by the formula: -OR⁴ [wherein R⁴ represents an alkyl group having 1 to 6 carbon atoms (e.g. methyl, ethyl, propyl, i-propyl, butyl, tert-butyl, hexyl)].

Esterified carboxyl groups represented by X^2 include those represented by the formula: -CO-OR 5 - [wherein R^5 represents a hydrocarbon residue which may be substituted], and the "hydrocarbon residues which may be substituted" represented by R^5 include the groups described above as "the hydrocarbon

residues which may be substituted" represented by R¹, R², R³, or X¹.

Amide-forming carboxyl groups represented by X² include those represented by the formula:

wherein R⁶ is a hydrogen atom or a hydrocarbon residue which may be substituted, and R⁷ is a hydrogen atom or a lower alkyl group. In the formula described above, the "hydrocarbon residues which may be substituted" represented by R⁶ include the "hydrocarbon residues which may be substituted" represented by R¹, R², R³, R⁵, or X¹, described above, and the lower alkyl groups represented by R⁷ include alkyl groups having 1 to 6 carbon atoms each (e.g. methyl, ethyl, n-propyl, i- propyl, n-butyl, i-butyl, tert-butyl, n-pentyl, n-hexyl). In the formula described above, R⁶ and R⁷ may constitute a cyclic amino group together with the adjacent nitrogen atom, and the cyclic amino groups formed by R⁶, R⁷, and the adjacent nitrogen atom include nitrogen-containing 5- to 7-membered heterocyclic groups, such as the groups represented by the formula:

those represented by the formula:

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and those represented by the formula:

In these formula, s represents 0, 1, or 2, t represents 1, or 2, and R⁸ represents a substituent which the cyclic amino group formed by the R⁶, and R⁷ may have, or a hydrogen atom; the substituents include alkyl groups having 1 to 3 carbon atoms each (e.g. methyl, ethyl, propyl), oxo, hydroxy, phenyl, benzyl, and amino groups.

The groups represented by the formula:

$$(\widehat{\underline{\mathbb{A}}}) - \mathbf{NH} - \widehat{\underline{\mathbf{C}}} - \widehat{\mathbf{C}} - \widehat{\underline{\mathbf{C}}}$$

as X1 when X1 represents an acyl group, and the groups represented by the formula:

as the substituted amino groups when X^2 represents an amide-forming carboxyl group, represent the residues of amino acid derivatives, where the amino acids are not specified. The amino acids may be of D-form or L-form. R^9 , R^{10} , and R^{11} are the same or different, each representing a hydrogen atom or a lower alkyl group which may be substituted. R^9 and R^{10} may bind to each other to form a lower alkylene chain represented by the formula: $-(CH_2)_m$ - (wherein m represents an integer of 2 to 4), and A represents a hydrogen atom, lower alkyl group, or acyl group.

The residues of amino acid derivatives described above include those of derivatives of amino acids such as glycine, alanine, glutamic acid, leucine, isoleucine, phenylalanine, aspartic acid, cysteine, sarcosine, glutamine, asparagine, and proline.

When the compound of the general formula (I) has an asymmetric carbon atom, the compound may be of D-, L- or DL-form, being unaffected by the asymmetry of the group represented by X^1 or X^2 .

Among the compounds represented by the formula (I) described above, those excellent in chemical stability are desirable, and R^1 and R^2 may be any group that has a steric effect contributing to stabilization of -SNO group, being desirably a C_{1-6} alkyl group such as methyl, ethyl, or propyl, phenyl, or naphthyl; when R^1 and R^2 are bound to each other, the group formed by R^1 and R^2 together with the carbon atoms to which the groups are bound is desirably cyclopentyl or cyclohexyl.

 ${
m R}^3$ is desirably a hydrogen atom, or a ${
m C}_{6-10}$ aromatic acyl group such as benzoyl, naphthoyl, or phenylacetyl. X¹ is desirably a hydrogen atom or an amino acid residue, and the amino acid is desirably glycine, aspartic acid, phenylalanine, asparagine, glutamic acid, or glutamine. ${
m X}^2$ is desirably carboxyl, carbonylamino, or carboxyl forming an amide with an amino acid residue, and the amino acid is desirably glycine, asparagine, glutamine, aspartic acid, glutamic acid, or phenylalanine.

Among the compounds represented by the formula (I) described above, are desirable those wherein each of R^1 and R^2 represents C_{1-6} alkyl group, phenyl, or naphthyl, or R^1 and R^2 form cyclopentyl or cyclohexyl together with the carbon atoms to which R^1 and R^2 are bound, R^3 is a hydrogen atom or a C_{6-10} aromatic acyl group, X^1 is a hydrogen atom or an amino acid residue of which amino acid is selected from the group consisting of glycine, aspartic acid, phenylalanine, asparagine, glutamic acid, and glutamine, X^2 is a carboxyl group, carbonylamino or a carboxyl group forming an amide with an amino acid residue of which amino acid is selected from the group consisting of glycine, aspartic acid, asparagine, glutamic acid, glutamine, and phenylalanine.

When the compound (I) of this invention is basic, the compound may form an acid adduct, especially a physiologically acceptable acid adduct; such adducts are exemplified by salts with inorganic acids (e.g. hydrochloric acid, nitric acid, phosphoric acid, hydrobromic acid), and salts with organic acids (e.g. acetic acid, propionic acid, fumaric acid, maleic acid, tartaric acid, citric acid, malic acid, oxalic acid, benzoic acid, methanesulfonic acid, benzoic acid).

The compounds of the general formula (I) can be produced by nitrosation of the compounds represented by the general formula (II).

$$X^{1} - \frac{R^{3}}{N^{2}} > CH - \frac{R^{1}}{C} - SH$$
 (II)

wherein R1, R2, R3, X1, and X2 mean the same as described above.

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Reagents generally used for the nitrosation of the compound (II) include nitrogen monoxide, nitrogen dioxide, dinitrogen tetraoxide, nitrosyl chloride, nitrous acid, and ethyl nitrite, but the reagents are not limited to these, and any reagent that can usually be used for nitrosation may be used.

The reaction may be conducted without any solvent or in a solvent. Any solvent may be used as far as it does not inhibit nitrosation, including water, alcohols (e.g. methanol, ethanol, propanol, butanol, tert-butanol), petroleum-composing solvents (e.g. n-hexane, n-pentane, n-heptane), aromatic solvents (e.g. benzene, toluene, pyridine), ethers (e.g. ethyl ether, tetrahydrofuran, dioxane, isopropyl ether), amides (e.g. N,N-dimethylformamide, N,N-dimethylacetamide), esters (e.g. methyl acetate, ethyl acetate, butyl acetate), halogenated hydrocarbons (e.g. dichloromethane, chloroform, dichloroethane, carbon tetrachloride), and dimethyl sulfoxide.

The reaction can be conducted at -30 °C to 150 °C, but is desirably conducted at a lower temperature (-5 °C to 30 °C). For one mole of the compound (II), desirably 1 to 5 moles of the nitrosating reagent are used. The reaction time varies depending on the properties of the compound (II) being generally 1 minute

to 6 hours, desirably as short as 1 minute to 30 minutes.

The compounds (II) can be produced according to the per se known method [Angewandte Chemie, 87, 372 (1975)], for example, by the procedures shown as the Reaction Formulas 1 to 4.

$$R^{1}$$

$$CII - CIIO + S_{2}CQ_{2} \longrightarrow R^{1}$$

$$CH_{2}$$

$$CH_{3}$$

$$CH_$$

wherein the symbols are the same as described above.

Reaction Formula 1

wherein R' is a $C_{1-5} {\rm lower}$ alkyl or benzyl, and other symbols are the same as described above.

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Reaction Formula 2

$$\frac{\text{IICM}}{R^2} > \frac{R^1}{C} - \text{CH} < \frac{\text{NH}_3}{CM} > \frac{R^1}{C} + \frac{\text{SH}}{CM} < \frac{\text{NH}_3}{CM}$$

$$\frac{\text{HCQ}}{\text{HOOC}} > \text{CH} - \frac{R^{1}}{C} - \text{SH} \cdot \text{HCQ} \qquad (\text{II a})$$

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wherein the symbols are the same as described above.

Reaction Formula 3

$$\begin{array}{c|c}
R^{1} & & S - CH_{2} \\
\hline
R^{2} & C - CHO
\end{array}$$

$$\begin{array}{c|c}
& & S - CH_{2} \\
\hline
R^{1} & C - CHO
\end{array}$$

$$\begin{array}{c|c} & S-CH_2 \\ \hline NH_3 & R^1 \\ \hline IICN & R^2 \\ \hline C-CH \\ \hline CN & IICO \\ \hline IICO & II_2N \\ \hline IICO & III_2N \\ \hline IICO & III_2N$$

$$\frac{\text{II}_{2} \dot{\text{N}}}{\text{HOOC}} > \text{CII} - \frac{\dot{\text{R}}'}{\dot{\text{C}}} - \text{SII} \cdot \text{HCQ} \qquad (\Box_{a})$$

wherein the symbols are the same as described above.

Reaction Formula 4

The compound (IIa) or (IIb) thus obtained is further subjected to N-acylation, N-alkylation, N-peptide formation, or esterification, alkylation, or peptide formation at the C terminal, to give the compound (II).

These reactions can be conducted according to the per se known method.

The compounds (I) of this invention act on the cardiovascular system of mammals, exerting excellent hypotensive action, anti-arrhythmic action, anti-anginal action, cardiotonic action, or coronary vasodilation.

The compounds (I) of this invention are excellent in duration and strength of the cardiovascular action as compared with the known nitro compounds such as nitroglycerine and nitrites, having no or only very mild undesirable side effects in the cardiovascular, psychic-nervous, or digestive system, such as dizziness, palpation, discomfort in the chest, arrhythmia, headache, fatigue, nausea, and vomiting. The compounds are remarkably effective after oral, parenteral, or percutaneous administration. Therefore the compounds are useful as therapeutics or prophylactics for various cardiovascular disorders in mammals including humans. Among the compounds (I) of this invention, those that dilate selectively the coronary vessels are useful as the prophylactics and therapeutics for angina pectoris.

The diseases for which the compounds (I) of this invention are useful include angina pectoris, myocardial infarction, cardiac asthma, achalasia (temporary remission), coronary sclerosis (chronic ischemic heart disease, asymptomatic ischemic heart disease, arteriosclerotic heart disease), maintaining hypotensive state during operation, emergency treatment of abnormal hypertension during operation, acute heart failure, essential hypertension, and renal hypertension; the compounds can be used for prevention and treatment of these diseases.

The compounds of this invention as such or a stabilized conjugate thereof with cyclodextrin, etc. can be administered to mammals including human orally or parenterally in various forms such as tablets, granules, capsules, injections, suppositories, percutaneous preparations, buccal preparations (sublingual tablets), ointments, and cataplasms. The dose varies depending on the type of the disease to be treated and the symptom, the daily dose being generally 0.1 mg to 500 mg, desirably 1 mg to 30 mg for oral administration to an adult human.

In this specification, amino acids, protective groups, and others are sometimes shown by conventionally used abbreviations based on the IUPAC-IUB Commission on Biological Nomenclature. The abbreviations used are listed in the following.

Ac: acetyl

Boc: t-butoxycarbonyl OBzl: benzylester

WSC: 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide

HOBt: 1-hydroxy-benzotriazole

Trt: trityl

Pen: penicillamine

Gly: glycine

Ala: alanine

Val: valine

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Leu: leucine Pro: proline

Phe: phenylalanine

Tyr: tyrosine

Glu: glutamic acid

Asp: aspartic acid

The side chains of amino acid residues are represented as follows:

$$\begin{array}{c} \vdots \\ \text{CH}_2 \\ \text{H}_2 \text{N} - \text{CH} - \text{COOH} \end{array}$$

EXAMPLES

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The following Reference Examples, Working Examples, Preparation Examples, and Experimental Examples explain this invention in more detail, but should not limit this invention.

Reference Example 1 (Synthesis of the Compound A-1)

To the solution of S-trityl-L-penicillamine (69.5 g) and di-t-butyldicarbonate (46.5 g) in dichloromethane (1500 ml), was added triethylamine (20.2 ml) at 0 °C, and the mixture was stirred at room temperature for 5 hours. To the reaction mixture were added ice and an aqueous solution of potassium hydrogensulfate. The organic layer was washed with an aqueous solution of potassium hydrogensulfate, water, and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, to give N-t-butoxycarbonyl-S-trityl-L-penicillamine (87.0 g).

In the same way the Compound A-2 listed in Table 1 described below was synthesized.

Reference Example 2 (Synthesis of the Compound B-1)

To the solution of N-t-butoxycarbonyl-S-trityl-D-penicillamine (A-2) (6.0 g) in dimethylformamide (40 ml), were added methyl iodide (1.5 ml) and potassium hydrogencarbonate (2.4 g), and the mixture was stirred for 14 hours. To the reaction mixture was added ice-water, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and then with saturated saline, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, to give N-t-butoxycarbonyl-S-trityl-D-penicillamine methyl ester (6.0 g).

Reference Example 3 (Synthesis of the Compound B-2)

To the solution of N-t-butoxycarbonyl-S-trityl-L-penicillamine (A-1) (4.0 g) and 1-hydroxy-benzotriazole (abbreviated as HOBt) (1.2 g) in chloroform (40 ml) and tetrahydrofuran (16 ml), was added dropwise by ice-cooling the solution of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (water-soluble carbodiimide: abbreviated as WSC) (1.7 g) in chloroform (10 ml). The mixture was stirred at the same temperature for 1 hour, to which glycine ethyl ester hydrochloride (1.1 g) and triethylamine (0.85 ml) were added, and the mixture was stirred at room temperature for 12 hours. After addition of water, the organic layer was washed with an aqueous solution of potassium hydrogensulfate, water, an aqueous solution of sodium hydrogencar-bonate, water and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, and the residue was subjected to column chromatography, to give N-t-butoxycarbonyl-S-trityl-L-penicillamylglycine ethyl ester (4.5 g).

In the same way the Compounds B-3 to B-22 and D-30 listed in Table 1 described below were synthesized.

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Reference Example 4 (Synthesis of the Compound C-2)

To the solution of N-t-butoxycarbonyl-S-trityl-L-penicillamylglycine ethyl ester (B-2) (4.5 g) and 2.6-lutidine (2.8 ml) in dichloromethane (100 ml), was added dropwise at 0°C the solution of trimethylsilyl trifluoromethanesulfonate (3.9 ml), and the mixture was stirred for 1 hour while the temperature was gradually returned to room temperature. To the reaction mixture was added ice-water, and the organic layer was washed with 1N-hydrochloric acid, water, an aqueous solution of sodium hydrogencarbonate, water, and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, to give S-trityl-L-penicillamylglycine ethyl ester (3.8 g)

In the same way the Compounds C-1, and C-3 to C-22 listed in Table 1 described below were synthesized.

Reference Example 5 (Synthesis of the Compound D-3)

To the solution of S-trityl-L-penicillamylglycine ethyl ester (C-2) (3.7 g) in dichloromethane (50 ml) were added acetyl chloride (0.66 ml) and triethylamine (0.88 ml) at 0 °C. The mixture was stirred at the same temperature for 15 minutes and then ice water was added. The organic layer was washed with an aqueous potassium hydrogensulfate solution, water, an aqueous sodium hydrogencarbonate solution, water and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, and the residue was subjected to silica gel column chromatography, to give N-acetyl-S-trityl-L-penicillamylglycine ethyl ester (3.5 g).

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Reference Example 6 (Synthesis of the Compound D-4)

To the solution of S-trityl-L-penicillamylglycine ethyl ester (C-2) (5.4 g) and N-t-butoxycarbonyl-L-glutamic acid- α -benzyl ester (3.8 g) in chloroform (100 ml) was added WSC (2.4 g) at 0 °C, and the mixture was stirred at room temperature for 3 hours. To the reaction mixture was added ice water. The organic layer was washed with an aqueous potassium hydrogensulfate solution, water, aqueous sodium hydrogencarbonate solution, water and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, and the residue was subjected to column chromatography, to give (4S)-4-t-butoxycarbonylamino-4-benzyloxycarbonylbutyryl-S-trityl-L-penicillamylglycine ethyl ester (8.4 g).

In the same way the Compounds D-1, D-2, D-5 to D-27 and D-29 listed in Table 1 described below were synthesized.

5 Reference Example 7 (Synthesis of the Compound E-5)

To the solution of (4S)-4-t-butoxycarbonylamino-4-benzyloxycarbonylbutyryl-S-trityl-L-penicillamyl-glycine ethyl ester (D-4) (8.4 g) in tetrahydrofuran (150 ml) was added 1N-sodlum hydroxide (25.3 ml) and

the mixture was stirred at room temperature for 2 hours. Tetrahydrofuran was evaporated off under reduced pressure, and the aqueous layer was washed twice with diethyl ether, to which an aqueous potassium hydrogensulfate solution was added to make it acidic, and the solution was extracted with ethyl acetate. The organic layer was washed with water and saturated saline, and the solvent was evaporated off under reduced pressure, to give $[N-\gamma-(N-t-butoxycarbonyl)-L-glutamyl-S-trityl-L-penicillamyl]glycine (7.0 g).$

In the same way the Compounds E-1 to E-4, and E-6 to E-32 listed in Table 1 described below were synthesized.

10 Reference Example 8 (Synthesis of the Compound F-5)

The solution of $[N-\gamma-(N-t-butoxycarbonyl)-L-glutamyl-S-trityl-L-penicillamyl]glycine (E-5) (3.0 g) in chloroform (60 ml) was bubbled with hydrogen chloride gas at 0 <math>^{\circ}$ C for 30 minutes. To the reaction mixture was added diethyl ether, and the crystals were collected by filtration and washed with diethyl ether. The crystals were dried under reduced pressure, to give $(N-\gamma-L-glutamyl-L-penicillamyl)glycine hydrochloride (1.7 g).$

In the same way the Compounds F-1 to F-4, and F-6 to F-32 listed in Table 1 described below were synthesized.

Reference Example 9 (Synthesis of the Compound B-23)

To the solution of N-t-butoxycarbonyl-S-trityl-L-penicillamine (A-1)(4.0g) and HOBt (1.2g) in chloroform (40ml) and tetrahydrofuran (15ml), was added dropwise under ice-cooling the solution of WSC (1.7g) in chloroform (10ml). The mixture was stirred at the same temperature for 1 hour, to which water was added, and the organic layer was washed with an aqueous solution of potassium hydrogensulfate, water, an aqueous solution of sodium hydrogencarbonate, water and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, to give HOBt ester.

To the solution of p-sulfophenylalanine (2.0g) in water (40mt), sodium hydrogencarbonate (2.1g) was added. To this solution, the solution of the HOBt ester synthesized as described above in dioxanel (40mt) was added, followed by addition of tetrabutylammonium hydrogensulfate (3.3g), and the mixture was stirred at room temperature for 1 hour. The solvent was evaporated off under reduced pressure and the residue was extracted with chloroform. The organic layer was washed with an aqueous solution of potassium hydrogensulfate, water and saturated saline, in this order, and dried over magnesium sulfate. The solvent was evaporated off under reduced pressure, to give tetrabutylammonium N-t-butoxycarbonyl-S-trityl-L-penicillamyl-P-sulfophenylalanine (7.5g).

In the same way the Compound D-28 listed in Table 1 described below was synthesized.

Reference Example 10 (Synthesis of the Compound C-23)

To the solution of tetrabutylammonium N-t-butoxycarbonyl-S-trityl-L-penicillamyl-p-sulfophenylalanine (B-23)(7.5g) and 2,6-lutidine (3.8m1) in dichloromethane (100m1), was added dropwise at 0°C the solution of trimethylsylyl trifluoromethanesulfonate (5.5mt), and the mixture was stirred for 1 hour while the temperature was gradually returned to room temperature. The solvent was evaporated off under reduced pressure and the residue was washed with diethyl ether and acetone, in this order, to give S-trityl-L-penicillamyl-p-sulfophenylalanine (3.1g).

Table 1 shows the structure, physical properties, and NMR data of the Compounds A-1 to F-32 synthesized in the Reference Examples.

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40

45

		1								F			
5		standard DCl3	44(9H),	14-7.34	.20(1H)	44(9H),	37(1H),	. 70		45(9H),	37(1H),	. 70	
10		NMR spectra TMS internal stand (6,ppm) in CDCl3	1.07(3H), 1.13(3H), 1.44(9H),	3.41(1H), 5.32(1H), 7.14-7.34	(9H), 7.50-7.70(6H), 8.20(1H)	1.06(3H), 1.12(3H), 1.44(9H),	3.46(1H), 4.90(1H), 5.37(1H),	7.10-7.36(9H), 7.56-7.70		1.02(2H), 1.07(3H), 1.45(9H),	3.54(1H), 3.36(3H), 5.37(1H),	7.10-7.33(9H), 7.53-7.70	
15			07(3H), 1	41(1H), 5	Н), 7.50-	06(3H), 1	46(1H), 4	10-7,36(H)	02(2H), 1	54(1H), 3	10-7.33((H
20		E G X	-:	3.	6)	_;	<i>د</i> .	7.	(H9)	7	3.	7.	(H9)
		Related Ref. Ex.								2			
25		Molecular formula Physical properties	C29H33NO4S	amorphous		3 NO.S	amorphous			C30H35NO.S	amorphous		
30		Mole form Phys prop	í	amo		C29H33NO4S	атол				amo		
	, 1 .	2	Trt			Trt				Trt			
35													
	Y — n∈	figuration $_{ m Y}$ of Pen	HO			НО				0Me			
40	% - P en -	igurati of Pen			····	Ω				Q		·	
45		Conf											
50	_		Вос			Вос	· · · · ·			Вос			·
55	able	Compound	A - 1			A-2				B-1			

5		(3H),	(2H),	(IH),	0(6H)	(3H),	(2H),	(111),	0(6H)	(3H),	(111),	(1H),	-		(3H),	3(1H),	'(1H),	5-7.38	
10		1.11(3H), 1.18(3H), 1.25(3H)	1. 42(9H), 3. 22(1H), 3. 96(2H),	4.17(2H), 5.34(1H), 6.20(1H),	7. 14-7. 34(9H), 7. 57-7. 70(6H)	1. 10(3H), 1. 13(3H), 1. 22(3H),	1. 42(9H), 3. 43(1H), 3. 95(2H),	4.14(2H), 5.47(1H), 6.53(1H),	7.11-7.34(9H), 7.57-7.70(6H)	1.06(3H), 1.13(3H), 1.24(3H),	1.38(3H), 1.43(9H), 3.38(1H),	4.15(1H), 4.49(1H), 5.36(1H),	6.38(1H), 7.14-7.40(9H),	(1)	0.88(3H), 0.92(3H), 1.05(3H),	1.16(3H), 1.42(9H), 2.13(1H),	3.31(1H), 3.66(3H), 4.47(1H),	5. 33(1H), 6. 34(1H), 7. 15-7. 38	73(6H)
15		1(3H), 1.1	2(9H), 3.2	7(2H), 5. 3	4-7.34(9H	0(3H), 1. 1	2(9H), 3.4	4(2H), 5. 4	1-7.34(91	16(3H), 1. 1	18(3H), 1.	5(1H), 4.	38(1H), 7.	7.56-7.70(6H)	38(3H), 0.	16(3H), 1.	31(1H), 3.	33(111), 6.	(9H), 7. 55-7. 73(6H)
20			1.4	4. 1	7.1	1:1	l. 4	4. 1	7. 1	1:	1.3	4. 1	6.	7.	0.		د	5.	(91
	-	3				3				3					8				
25		C33H+0N2OsS	amorphous			CaaHtoN2OsS	amorphous.	-		C3+H+2N2O5S	amorphous				C35H++N2O5S	amorphous		· · - ·	
30		C33H4	атог			CaaH+	amor			C3 + H+	amor				CasH+	amo			
		Trt	-			Trt				Tr					Trt				
35		Gly-OEt				Gly-OEt				L-Ala-OEt					L-Val-OMe		-		
40		3				5					· ·				<u> </u>				
	_					۵													
45	(continued)																		
50		Вос				Вос				Boc					Вос				
55	Table	B-2				B-3				B -4					B-5			-	

55	50	45	40		35	30	25		20	15	10	5	
Table	-1	(continued)			I								
8-6	Boc			L-Val-OMe	Me Trt	C35H4+N2O5S	205	~	0.87(3	87 (3H), 0. 90 (3H), 1. 05 (3H)	3H), 1.05	(3H),	ſ
						amorphous	snou		1.17(3H),	H), 1. 43(1. 43(9H), 2. 12(1H),	(1H),	
		— <u>.</u>					*******		3, 29(1	3. 29(1H), 3. 70(3H), 4. 48(1H),	3H), 4.48	(1H),	
									5.34(1	5.34(1H), 6.37(1H), 7.16-7.38	1H), 7.16	-7.38	
									(9H), 7	(9H), 7. 58-7. 68(6H)	(84)		
B-7	Вос			L-Leu-OEt	Et Trt	C37H48N2O5S	20.5	3	0.91(6	0.91(6H), 1.02(3H), 1.14(3H),	3H), 1.14	(3H),	
						amorphous	ons.		1, 22(3	22(3H), 1. 42(9H), 1. 30-1. 80	9H), 1.30	-1.80	
									(3H), 3	(3H), 3. 45(1H), 4. 13(2H), 4. 55	4.13(2H)	, 4.55	
									(1H), 5	(1H), 5. 33(1H), 6. 23(1H), 7. 10-	6.23(1H)	, 7. 10-	
									7.40(9	7.40(9H), 7.50-7.75(6H)	7.75(6H)		
B-8	Вос		٦	L-Pro-OMe	Me Trt	C35H42N2O5S	205	3	1.12(3	1. 12(3H), 1. 14(3H), 1. 44(9H),	3H), 1.44	(9H),	
						amorphous	snot		1.82 - 2	1.82-2.32(4H), 3.27-3.66(2H),	3. 27-3. 6	6(2H),	
									3.64(3	3.64(3H), 3.97(1H), 4.47(1H),	1H), 4.47	(1H),	
									5.40(1	40(1H), 7.12-7.33(9H),	7.33(9H)	•	
									7.56-7	56-7.66(6H)			
B-9	Boc			L-Phe-OEt	Et Trt	C+OH+BN2OsS	205	က	1.03(3	1. 03(3H), 1. 09(3H), 1. 16(3H),	3H), I. 16	(3H),	
						amorphous	snot		1.43(9	1. 43(9H), 3. 07(2H), 3. 20(1H),	2H), 3.20	(1H),	
									4.09(2	4.09(2H), 4.81(1H), 5.29(1H),	1H), 5.29	(IH),	
									6.29(1	29(1H), 7.04-7.38(14H)	7.38(14H	,'	
									7.52-7	52-7.73(6H)			
	: : : : : : : : : : : : : : : : : : : :												

55	50	45	40	35		30	25	20	15		10	5	
rable	~	(continued)											ſ
8-10	Boc			L-Tyr-OEt	Trt (C+0H+8N2O6S	S°	3	1.02(3H),), 1.07(3H)), 1. 18(3!!)	(311),	
						amorphous	ns.		1.44(911),), 2. 98(2H), 3. 26(1H)), 3. 26((IH),	
						ı	<u>-</u>		4.09(2H), 4.75(1H), 5.39(1H),	4.75(1H), 5.39((111),	
					_				5.87(1H),	87(1H), 6. 63(2H), 6. 94(2H)), 6.94((211),	
					-				7.12-7.32(10H), 7.55-7.64(6H)	(10H), 7	. 55-7. 6	34(6H)	
			1	T OEt	-				1. 04(3H), 1. 17(3H), 1. 24(6H),	1.17(31), 1. 24((ен),	
B-11	သလ			L-G1u-0Et	Trt (C30 H+0 N207S	2,5	~	1. 43(911), 1. 80-2. 50(411), 3. 23	1.80-2.	50(411),	3.23	
 : :		-				amorphous	us		(1H), 4.09(2H), 4.15(2H), 4.54	(2H), 4.	15(2H),	4.54	
						4			(1H), 5. 32(1H), 6. 38(1H), 7. 13-	(111), 6.	38(1H),	7.13-	
									7. 34(9H), 7. 57-7. 67(6H)	7.57-7.	67(6H)		
B13	Boc	:		MICHPh2	Trt	C+2H++N2O3S	35	3	0.98(311),	1.15(3H), 1.41(9H),	1), 1. 41	(дн),	
	, ,					m. p. 158.0-	I		3.60(1H), 5.29(1H), 6.15(1H),	5.29(1F	1), 6. 15	(111),	
			•			159.0			6.41(1H),	7.12-7.34(9H), 7.48-	34(9H),	, 7.48-	
									7.58(6H)				
			+		1				(110)00	10/0,	1	(10)	$\neg \neg$
B-13	Вос			-0Bz1	<u>.</u> .	C+7Hs0N2O7S	S,	<u></u>	1.05(3H),	1. 12(31	1. 12(3H), 1. 41(9H)	(A H)	
				L-ASp-0Bz1		amorphous	ns	 .	2.85(1H),	85(1H), 2.94(2H), 4.80(1H),	H), 4.80	(1H),	
						ı			5.02(2H),	02(2H), 5.07(2H), 5.25(1H)	1), 5. 25	(IH),	
									6.11(111),	11(1H), 7.12-7.40(19H),	40(19H	``	
			•		 -	1			7.56-7.67(6H)	(H9)			\neg

																1					\neg
5	(110)	(3H),	43(9H), 1.25-2.24(2H), 2.05(3H),	(2H),	(IH),	7(6H)	(3H),	35-1.52(2H), 1.42(9H), 1.86(1H),	((IH))	32(1H), 6.38(1H), 7.15-7.42(9H),		(0 H),	5(1H),	1),		0.82-0.91(6H), 1.05(3H), 1.15(3H),	1. 24(3H), 1. 42(9H), 1. 30-1. 81(3H),	3. 34(1H), 4. 14(2H), 4. 51(1H), 5. 33	33(9H),		
10	\\\\\\	06(3H), 1.17(3H), 1.24(3H),	5-2.24(2H)	50(2H), 3.22(1H), 4.16(2H),	4. 61(1H), 5. 31(1H), 6. 40(1H),	15-7.40(9H), 7.57-7.67(6H)	89(6H), 1.03(3H), 1.16(3H),), 1.42(9H)	3.34(1H), 3.66(3H), 4.52(1H),	8(1H), 7.15		98(3H), 1.15(3H), 1.41(9H)	3.60(1H), 5.28(1H), 6.15(1H),	6. 40(1H), 7:10-7.40(19H),), 1. 05(3H)	2(9H), 1.30	4(2H), 4.5	(1H), 6. 13(1H), 7. 15-7. 33(9H),		
15		16(3H), 1. I	13(9H), 1.2	0(2H), 3.2	31(1H), 5.3	5-7.40(9H	39(6H), 1.0	35-1.52(2H	34(1H), 3.6	32(1H), 6.3	53-7.73(6H)	38(3H), 1. 1	30(1H), 5.2	40(1H), 7:1	7. 48-7. 57 (6H)	82-0.91(6H	24(3H), 1. 4	34(1H), 4. 1	Н), 6. 13(1Н	7.56-7.63(6H)	
20		_;	-;	2:	4. (7.	0. 8	_;	^د .	57.	7.	0.	د	9.	7.	0.	- i	س		· ·	
		က					3					က				3					
25		C36H+6N2O5S2	amorphous		-		CasH+BN2OsS	amorphous	ı			C+2H++N2O3S	58.0-	159.0		C37H48N2O5S	amorphous				
30		Coe H+	amor				C36H4	amor				C+2H+	m. p. 158.0-	_		1					
35		L-Met-OEt Trt				_	L-Ile-OMe Trt					Ph2 Trt				L-Leu-OEt Trt					
40	-	L-Me					1-1					NHCHPh2				L-Le	···				
												Q				0					·
45	(continued															1					
50		Вос					Вос					Вос				Boc	, , :				
55	Table	8-14					B-15		<u> </u>			B-16				B-17					

	,				
5		0. 99(3H), 1. 11(3H), 1. 14(3H), 1. 42(9H), 2. 93-3. 16(2H), 3. 34(1H), 4. 08(2H), 4. 77(1H), 5. 27(1H), 5. 32(1H), 7. 08-7. 33(14H), 7. 54-7. 63(6H)	1. 08(3H), 1. 17(3H), 1. 20(3H), 1. 25(3H), 1. 42(9H), 1. 82-2. 43(4H), 3. 20(1H), 4. 07(2H), 4. 16(2H), ³ ; 4. 53(1H), 5. 34(1H), 6. 39(1H), 7. 15-7. 36(9H), 7. 56-7. 68(6H)	1. 12(3H), 1. 34(3H), 1. 41(9H), 2. 06(1H), 3. 68-4. 10(2H), 3. 76(3H), 4. 38(1H), 5. 21(1H), 6. 06(1H), 7. 19-7. 38(10H), 7. 63-7. 73(6H)	0. 94(6H), 1. 45(9H), 1. 80-2. 22(4H), 3. 43-3. 91(2H), 3. 70(3H), 4. 38-4. 49 (2H), 5. 43(1H), 7. 10-7. 32(9H), 7. 51-7. 63(6H)
10		11(3H), 1. 93-3. 16(2H) 77(1H), 5. 98-7. 33(1H)	17(3H), 1. 42(9H), 1. 07(2H), 4. 34(1H), 6. H), 7. 56-7.	34(3H), 1 68-4. 10(2) 21(1H), 6 0H), 7. 63-7	45(9H), 1. 8 H), 3. 70(3H), 7. 10-7. H), 7. 10-7. H)
15		0. \$9(3H), 1. 11(3H), 1. 14(3H), 1. 42(9H), 2. 93-3. 16(2H), 3. 34 4. 08(2H), 4. 77(1H), 5. 27(1H), 6. 32(1H), 7. 08-7. 33(14H), 7. 54-7. 63(6H)	1. 03(3H), 1. 17(3H), 1. 20(3H), 1. 25(3H), 1. 42(9H), 1. 82-2. 43 3. 20(1H), 4. 07(2H), 4. 16(2H), 4. 53(1H), 5. 34(1H), 6. 39(1H), 7. 15-7. 36(9H), 7. 56-7. 68(6H)	1. 12(3H), 1. 34(3H), 1. 41(9H), 2. 06(1H), 3. 68-4. 10(2H), 3. 76(4. 38(1H), 5. 21(1H), 6. 06(1H), 7. 19-7. 38(10H), 7. 63-7. 73(6H)	0. 94(6H), 1. 45(9H), 1. 80-2. 22(33. 43-3. 91(2H), 3. 70(3H), 4. 38-(2H), 5. 43(1H), 7. 10-7. 32(9H), 7. 51-7. 63(6H)
20		0. 1. 6. 7.	1. 1. 3. 4.	7	0. 3. (2
		က	က	ന	<u>ო</u>
25		C,oH,oN2OsS amorphous	CoeHteN2O7S amorphous	C3+H+0N2O6S amorphous	CasH+2N2OsS amorphous
30		O	O		
		T (1)	1. 1. 1.	- C	——————————————————————————————————————
35		L-Phe-0Et	∟0Et L-61u-0Et	L-Ser-OMe	L-Pro-OMe
40	d)		a		۵
45	(continued)				
50	1 (c	Вос	80 c	Вос	Вос
55	Table	8 - 1 8	B - 1 - 8	B-20	B-21

5		(H	. 2
	17(3H) 00(2H) 27(2H) 29(1H) 05(2H)	1. 07(3H (9H), 1. 75(1H (H),	63(2H), 12-7.3
10	0(3H), 1. 3(9H), 3. 7(2H), 4. 3(1H), 5. 8(2H), 7.	05(3H), H), 1. 43), 4. 62-), 6. 37(H), 7. 56- H), 7. 56-	1(3H), 1. 4(3H), 7. 58(6H)
15	1. 03(3H), 1. 10(3H), 1. 17(3H), 1. 30(3H), 1. 43(9H), 3. 00(2H), 3. 16(1H), 4. 07(2H), 4. 27(2H), 4. 58(2H), 4. 73(1H), 5. 29(1H), 6. 27(1H), 6. 78(2H), 7. 05(2H), 7. 12-7. 30(9H), 7. 55-7. 64(6H)	0. 92(12H), 1. 05(3H), 1. 07(3H) 1. 23-1. 66(16H), 1. 43(9H), 3. 02-3. 26(1H), 4. 62-4. 75(1H), 5. 36-5. 45(1H), 6. 37(1H), 7. 10-7. 43(12H), 7. 56-7. 78(8H)	1. 07(3H), 1. 11(3H), 1. 63(2H), 2. 33(1H), 3. 54(3H), 7. 12-7. 32 (9H), 7. 56-7. 68(6H)
20	1. 03 1. 30 3. 16 4. 58 6. 27 7. 12	0. 92 1. 23 3. 02 5. 36 7. 10	1.07 2.33 (9H),
	က	Cr.	4
25	C++Hs2N2OsS amorphous	Cs.Hr.NsOaSz amorphous	N02S
30		[C25H27NO2S 0ily
	F-	F -	[
35	CH2COOEt Tyr-OEt	SO3 · Bu + N - Phe - OH	Оже
40			
nued)			
\$ Continue			
50	Вос	Boc	
Table	8-22	8 - 23	1-0
55			

5	3H), 2H), 7. 34	3H), 2H), 7.37	3H), 1H), 1H), (6H)	3H), 1H), 1H),
10	. 24(3H), 1. 27(3H), 1. 29(3H), . 64(2H), 1. 81(2H), 3. 87(2H), . 16(2H), 6. 95(1H), 7. 13-7. 34 9H), 7. 63-7. 73(6H)	1. 25(3H), 1. 27(3H), 1. 29(3H), 1. 62(2H), 1. 80(1H), 3. 88(2H), 4. 16(2H), 6. 96(1H), 7. 16-7. 37 (9H), 7. 62-7. 73(6H)	1. 23(3H), 1. 24(3H), 1. 26(3H), 1. 30(3H), 1. 62(2H), 1. 78(1H), 4. 14(2H), 4. 39(1H), 6. 84(1H), 7. 15-7. 36(9H), 7. 63-7. 73(6H)	0. 84(3H), 0. 87(3H), 1. 25(3H), 1. 26(3H), 1. 64(2H), 1. 79(1H), 2. 10(1H), 3. 68(3H), 4. 36(1H), 6. 80(1H), 7. 14-7. 34(9H), 7. 62-7. 73(6H)
15	1. 24(3H), 1. 27(3H), 1. 64(2H), 1. 81(2H), 1. 16(2H), 6. 95(1H), (9H), 7. 63-7. 73(6H)	25(3H), 1. 27(3H), 62(2H), 1. 80(1H), i. 16(2H), 6. 96(1H), (9H), 7. 62-7. 73(6H)	3H), 1. 24(3H), 1. 62(2H), 4. 39(7. 36(9H),	0. 84(3H), 0. 87(3H), 1. 25(1. 26(3H), 1. 64(2H), 1. 79(2. 10(1H), 3. 68(3H), 4. 36(6. 80(1H), 7. 14-7. 34(9H), 7. 62-7. 73(6H)
20	1. 24(1. 64(4. 16((9ll),	1. 25(1. 62(4. 16((9H),	1. 23 (1. 30 (4. 14 (7. 15-	0.84(1.26(2.10(6.80(7.62-
	4	4	73"	4
25	C28H32N2O3S amorphous	C2.8 H3.2 N2.03.S amorphous	C.sHs.N.OsS amorphous	amorphous
30	Trt C28Ha	Trt C28H2	Trt C29H	Trt C3.0113.6N203S amorphous
35	Gly-0Et	Gly-OEt	L-Ala-OEt	L-Val-OMe
40		Q		
45 .	(continued)			
50	i		=	=
	C-2	C - 3		ما ا

5	(3H), (1H), (1H),	1. 24 (2H), 4. 49 (9H),	2. 22 2. 96 7. 05-	3H), 2H), 1H), (6H)
10	3H), 1. 24(1H), 2. 06(3H), 4. 31(7. 36(9H),	1. 23(6H), (3H), 1. 65 2H), 4. 36- 7. 14-7. 35	3H), 1. 60- 2. 61(1H), 4. 35(1H), 7. 78(6H)	3H), 1. 19(1H), 3. 00(1H), 6. 67(7. 59-7. 70
15	0. 83(3H), 0. 86(3H), 1. 24(3H), 1. 29(3H), 1. 80(1H), 2. 06(1H), 2. 09(2H), 3. 69(3H), 4. 31(1H), 6. 67(1H), 7. 16-7. 36(9H), 7. 64-7. 73(6H)	0.80-1.00(6H), 1.23(6H), 1.24 (3H), 1.35-1.73(3H), 1.65(2H), 1.84(1H), 4.12(2H), 4.36-4.49 (1H), 6.73(1H), 7.14-7.35(9H), 7.61-7.73(6H)	1. 29(3H), 1. 34(3H), 1. 60-2. 22 (4H), 1. 84(2H), 2. 61(1H), 2. 96 (2H), 3. 63(3H), 4. 35(1H), 7. 05- 7. 42(9H), 7. 50-7. 78(6H)	1. 08(3H), 1. 18(3H), 1. 19(3H), 1. 58(2H), 1. 62(1H), 3. 00(2H), 4. 11(2H), 4. 69(1H), 6. 67(1H), 7. 01-7. 38(4H), 7. 59-7. 70(6H)
20	0. 8. 2. 0 6. 6. 67	0.8(3H) (3H) 1.84 (1H) 7.61	1. 29 (4H) (2H) 7. 42	1. 08 1. 58 4. 11 7. 01
	च	4.	4	4
25	CsollseN2OsS amorphous	amorphous	ooffotN2OoS amorphous	amorphous
30	S	O	S	၁
		F-	Trt	Trt
35	L-Val-041c	L-Leu-OEt	L-Pro-OMe	L-Phe-OEt
40				
	<u>a</u>			
ه، (continued				
50	===	=	: :==:	· <u></u>
Table	6 - 6	C-7	8- 0	0 - 0
	·			L

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	3H),	2H), IH),	7.33		211),	4.10	6.98	-7.72		2H),	7.32			2H),	1117,	7(64)	\ ;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;	
	3H), 1. 18((LH), 2. 93(; LH), 6. 67(ZII), 7. 10-′	(H9)	6H), 1.64(2.43(4H),	4.42(1H),	(9H), 7.63		3H), 1. 62(1H), 7.10-	(H9)0		1H), 1. 58(1H), 4. 76(6.91(18/), 7.55-7.7		
)H), 1. 09(3	2H), 1. 63(2H), 6. 95(1	7. 60-7.70	5H), 1. 24(1H), 1.80-	4.14(2H),	7, 15-7, 36		3H), 1. 21(1H), 6.07(7.60-7.7		6H), 1.50(1H), 3.04(5. IT (4H),	1.44(L311)	
	0.26(9	1.60(2	6.75(2	(9H),	1.23(1.84((2H),	(1H),	(911)	1.20(1.97((20H)		1.17(2.72(4. 95	00.7	
	4					7				4				4				
	0,581	sno				0.5	sno			205	ons			2058	snor			
	C30H46N2	amorph				C33H40N2	amorph			Ca, Hae N	amorph	•		C+2H+2N	amorph			
-	Tr					Trt				Trt				Trt				
					-0Et					IPh2				-0Bz1	-082 I			
	Si L-Ty					1-0-7				NHCF					-\-\-			
														-1				
ontinued)																		- 1
1 (00	: ==	1					:			=	:			æ				
Table	C-10	· ·			-					C-13				C-13				
	1 (co	(continued) SiMes	SiMes SiMes L-Tyr-OEt Trl CsellseN2O.SSi 4 Camorphous	SiMes SiMes Continued) L L-Tyr-OEt Trt CsellseN20,5Si 4 6	SiMes SiMes L-Tyr-OEt Trl CsellsN2O1SSi 4	SiMe3 SiMe3 SiMe3 4 (C3.011.6N20.5Si 4 (Cantinued) L-Tyr-OEt Trl C3.011.6N20.5Si 4 (Cantinued) Trl C3.011.6N20.5Si 4 (Cantinued) Cantinued) Cantinued Cantin		(continued) SiMe3		(continued) SiMe3		(continued)	(continued)					

5	1. 84(1H), 2. 44(2H), 1H), (6H)	(3H), 2H), 1H),	2H), 7.35 8(6H)	3H), 1.61(2H), 1H),
10	1. 63(2H), 2. 05(3H), 1H), 7. 01(0.96-1.93 3H), 1.61(3H), 4.41(7.38(9H),	3H), 1.59(1H), 7.06- , 7.58-7.6	3H), 1. 25(1. 74(3H), 2H), 4. 38(7. 37(9H),
15	1. 12-1. 34(9H), 1. 63(2H), 1. 84(1H), 1. 80-2. 20(2H), 2. 05(3H), 2. 44(2H), 4. 16(2H), 4. 52(1H), 7. 01(1H), 7. 13-7. 42(9H), 7. 56-7. 79(6H)	0. 73-0. 94(6H), 0. 96-1. 93(3H). 1. 04(3H), 1. 17(3H), 1. 61(2H), 1. 79(1H), 3. 68(3H), 4. 41(1H), 6. 82(1H), 7. 14-7. 38(9H), 7. 56-7. 74(6H)	1. 21(3H), 1. 22(3H), 1. 59(2H), 1. 96(1H), 6. 06(1H), 7. 06-7. 35 (19H), 7. 53(1H), 7. 58-7. 68(6H)	0.88(6H), 1.23(3H), 1.25(3H), 1.28(3H), 1.40-1.74(3H), 1.61(2H), 1.88(1H), 4.13(2H), 4.38(1H), 6.81(1H), 7.15-7.37(9H), 7.57-7.72(6H)
20	1. 12- 1. 80- 4. 16(0. 73- 1. 04(1. 79(6. 82(7. 56-	1. 21(1. 96((19H)	0.88(1.28(1.88(6.81(7.57-
	4	4	4	7
25	C3.H3.N2O3S2 amorphous	ColHosN2OoS amorphous	37H36N2OS amorphous	C32H40N2O3S amorphous
30			0	C32H+c
	. L	Trt	Trt	F-1
35	L-Met-OEt	L-11e-0Me	NIICHPh.	L-Leu-OEt
40	ے		۵	
45				
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50	7	In	9	
E (C-14	C-13	C-16	C-17

5	H), H), H), (6II)	H), .42(4H), H),	8. 98(2II), (H), (6H)	2. 12(4H), 3. 32(2H), (6H)
10	1. 17(3H), 1. 20(3H), 1. 23(3H), 1. 48(2H), 1. 71(1H), 3. 00(2H), 4. 10(2H), 4. 65(1H), 6. 88(1H), 7. 00-7. 36(14H), 7. 67-7. 72(6H)	. 23(3H), 1. 24(6H), 1. 27(3H), . 60(2H), 1. 82(1H), 1. 80-2. 42(4H), . 08(2H), 4. 14(2H), 4. 39(1H), .; 97(1H), 7. 14-7. 36(9H)	0. 08(9H), 1. 27(3H), 1. 29(3H), 1. 62(2H), 1. 67(1H), 3. 61-3. 98(2H), 3. 68(3H), 4. 50(1H), 6. 79(1H), 7. 15-7. 37(9H), 7. 65-7. 74(6H)	05(3H), 1. 31(3H), 1. 60-2. 12(4H), 82(2H), 2. 90(1H), 2. 90-3. 32(2H), 68(3H), 4. 25-4. 32(1H), 12-7. 34(9H), 7. 57-7. 68(6H)
15	17(3H), 1.20 18(2H), 1.71 10(2H), 4.65 00-7.36(14H)	23(3H), 1. 24(6H), 1. 27 60(2H), 1. 82(1H), 1. 80 08(2H), 4. 14(2H), 4. 39 97(1H), 7. 14-7. 36(9H) 62-7. 73(6H)	08(9H), 1. 2. 62(2H), 1. 6 68(3H), 4. 5 15-7. 37(9H	05(3H), 1. 3 82(2H), 2. 9 68(3H), 4. 2 12-7. 34(9H
20	1 4 5	1. 1. 4	0. 1. 3.	7.3.7.
	4	4	4	4
25	CasHasN2OaS amorphous	C33H40N2O5S Oily	C32H40N2O4SSi amorphous	C30H3+N2O3S amorphous
30	Cosll amo	C3 3 H	C3 2 H	C30F
	T-	T T		T t
35	L-Phe-OEt	L-Glu-0Et	Si(Me)s L-Ser-OMe	L-Pro-OMe
40	0	0		0
55 Continued)				
50		= .	=	
ا د ح ح	⊗ 1	6 0	C-20	C-21
55	L			

	5 <i>0</i>	45	40	35		25 30		20	15	5
Table		l (continued)								
C-22			<u> </u>	ÇII2COOEt Tyr-OEt	Trt	Trt Cooffee No Os Samorphous	4	1. 09(3H), 1. 18(1. 31(3H), 1. 55(2. 95(2H), 4. 11(4. 60(2H), 4. 53- 6. 82(2H), 7. 01(7. 58-7. 69(6H)	1. 09(3H), 1. 18(3H), 1. 20(3H), 1. 31(3H), 1. 55(2H), 1. 64(1H), 2. 95(2H), 4. 11(2H), 4. 28(2H), 4. 60(2H), 4. 53-4. 76(1H), 6. 6, 6. 82(2H), 7. 01(2H), 7. 07-7. 3 7. 58-7. 69(6H)	1. 09(3H), 1. 18(3H), 1. 20(3H), 1. 31(3H), 1. 55(2H), 1. 64(1H), 2. 95(2H), 4. 11(2H), 4. 28(2H), 4. 60(2H), 4. 53-4. 76(1H), 6. 69(1H), 6. 82(2H), 7. 01(2H), 7. 07-7. 31(9H), 7. 58-7. 69(6H)
C-23	==		`	\$0°111 DI,-Phe-011	L. (Trt CaaHa+N2OgSz amorphous	01	*0.99(3H), 1.11 2.10(1H), 3.01(7.16-8.52(22H)	, 1. 11(3H) 3. 01(2H), (22H)	*0.99(3H), 1.11(3H), 2.09(2H), 2.10(1H), 3.01(2H), 4.39(1H), 7.16-8.52(22H)
0-1	Boc-L·C	D-1 Boc-L-Glu-0B21	Q	ОЖе	Trt	C.z.H.sN2O,S amorphous	9	1. 01(3H), 1. 12(1. 70-2. 45(4H), (1H), 4. 35(1H), (1H), 6. 54(1H), 7. 54-7. 62(6H)	1. 12(3H), (4H), 3. 65 (1H), 5. 16 (1H), 7. 13 (6H)	1. 01(3H), 1. 12(3H), 1. 41(9H), 1. 70-2. 43(4H), 3. 65(3H), 3. 85 (1H), 4. 35(1H), 5. 16(2H), 5. 34 (1H), 6. 54(1H), 7. 13-7. 37(14H), 7. 54-7. 62(6H)
D-2	Boc -D -Glu-OMc	11a-0Mc	Q	ОМе	<u></u>	Trt CasH++N2O7S amorphous	9	1. 02(3H), 1. 13 1. 70-2. 45(4H) (3H), 3. 81(1H) (1H), 6. 38(1H) 7. 53-7. 68(6H)	1. 13(3H), (4H), 3. 68 (1H), 4. 33 (1H), 7. 14 (6H)	1. 02(3H), 1. 13(3H), 1. 44(9H), 1. 70-2. 45(4H), 3. 68(3H), 3. 72 (3H), 3. 81(1H), 4. 33(1H), 5. 29 (1H), 6. 38(1H), 7. 14-7. 32(9H), 7. 53-7. 68(6H)

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5		5(3H), 5(2H), 7, 7, 16-	(3H), , 3.57 , 4.33 , 6.23 (4(14H),	55(111), 1(111), 1(111), 5. 1-1, 1, 6. 87(111), 16(611)	5(3H), 1. 4 53(1H), (2H), 4. 3 1, 6. 48(1H)
10		1. 11(3H), 1. 15(3H), 1. 25(3H), 1. 98(3H), 3. 77(1H), 3. 95(2H), 4. 18(2H), 6. 23-6. 36(2H), 7. 16- 7. 35(9H), 7. 58-7. 67(6H)	1. 12(3H), 1. 19(3H), 1. 25(3H), 1. 41(9H), 1. 55-2. 26(4H), 3. 57 (1H), 3. 94(2H), 4. 17(2H), 4. 33 (1H), 5. 12(2H), 5. 38(1H), 6. 23 (1H), 6. 36(1H), 7. 14-7. 44(14H) 7. 54-7. 76(6H)	1. 13(3H), 1. 17(3H), 1. 21(3H), 1. 39 (9H), 1. 52-2. 32(4H), 3. 65(1H), 3. 91(2H), 4. 12(2H), 4. 29(1H), 5. 14 (2H), 5. 46(1H), 6. 52(1H), 6. 87(1H), 7. 10-7. 44(14H), 7. 46-7. 76(6H)	1. 12(3H), 1. 20(3H), 1. 25(3H), 1. 42 (9H), 1. 48-2. 36(4H), 3. 63(1H), 3. 68(3H), 3. 94(2H), 4. 17(2H), 4. 30 (1H), 5. 34(1H), 6. 26(1H), 6. 48(1H), 7. 15-7. 34(9H), 7. 57-7. 67(6H)
15		11(3H), 1. 1 98(3H), 3. 7 18(2H), 6. 2 35(9H), 7. 5	12(3H), 1. 19 41(9H), 1. 55 H), 3. 94(2H) H), 5. 12(2H) H), 6. 36(1H) 54-7. 76(6H)	13(3H), 1. 1 H), 1. 52-2. 91(2H), 4: 1 H), 5. 46(1H)	1. 12(3H), 1. 20(3H), 1. 25(3H), (9H), 1. 48-2. 36(4H), 3. 63(1H), 3. 68(3H), 3. 94(2H), 4. 17(2H), (1H), 5. 34(1H), 6. 26(1H), 6. 48
20		5 1. 1. 7. 7.	6 1. 1. 2. 2. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7.	6 (9 3. (2 (2 (7 (2 (2 (2 (2 (2 (2 (2 (2 (2 (2 (2 (2 (2	6 (9 (1) 1) 1 / 1 / 1 / 1 / 1 / 1 / 1 / 1 /
25		CoolloaN2OaS amorphous	CisHsaMaOaS amorphous	C.slisaNaOaS amorphous	Cas II to Na Oo S amorphous
30		Trt Cooll	Trt C,s H.	Trt C ₊ sii.	Trt Cas II.
35		Gly-OEt T	Gly-OEt T	Gly-OEt T	Gly-OEt T
40			ì	Ω	Q
45	1 (continued)	Λc	Boc-L-Glu-0Bz1	F80c-L-Glu-0Bz1	Poc-D-Glu-OMe
50	Table	0-3	D-4 Bc	D-5 Bo	D-6 Bc

	0 0 7	35, 00	61 (),	1 1 0
5	1. 4 3 (11H 6. 3),	1. 3 , 3. (2H -7.	1. 3 1. 3. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.	1. 4 4. 4 3(1F
	1. 12(3H), 1. 15(3H), 1. 24(3H), 1. 40 (9H), 1. 80-2. 20(2H), 2. 35-2. 63 (2H), 3. 51(1H), 3. 92(2H), 4. 10(1H), 4. 15(2H), 5. 10(2H), 5. 34(1H), 6. 34 (1H), 6. 94(1H), 7. 14-7. 37(14H), 7. 58-7. 67(6H)	1. 10(3H), 1. 18(3H), 1. 24(3H), 1. 39 (9H), 2. 62-2. 96(2H), 3. 51(1H), 3. 9G (2H), 4. 12(2H), 4. 52(1H), 5. 14(2H), 5. 74(1H), 6. 20-6. 35(2H), 7. 14-7. 35 (14H), 7. 56-7. 66(6H)	1. 09(3H), 1. 15(3H), 1. 23(3H), 1. 34 (3H), 1. 42(9H), 1. 65-2. 28(4H), 3. 61 (1H), 4. 14(2H), 4. 33(1H), 4. 44(1H), 5. 12(2H), 5. 38(1H), 6. 24(1H), 6. 38 (1H), 7. 14-7. 44(14H), 7. 58-7. 68(6H)	0. 85(3H), 0. 89(3H), 1. 12(3H), 1. 21 (3H), 1. 42(9H), 1. 70-2. 28(5H), 3. 39(1H), 3. 65(3H), 4. 36(1H), 4. 41 (1H), 5. 09(2H), 5. 46(1H), 6. 19(1H), 6. 46(1H), 7. 15-7. 41(14H), 7. 59- 7. 69(6H)
	4(3 35-), 4 4(1 37(4(3 51(), 5), 7	3(3) 28(28(1), 4 14(1)	28(28(36() 1), (11), (
10	1. 2 2. 2. (2H 5. 3	1. 2 , 3. (1H (2H	1. 2 -2. ((1H) ((1H) 6. 2	1. 1 1. 2 3 – 2. 4. 3 5 (14 1 (14
	1), 2H), 92, H), H),	H), 2H) . 52 . 35 (6H	H), . 65 . 33 H),	(H), (H), (H), (H), (141,
	5(3)	8(3 96(), 4 0-6	5(3), 4), 4 (1 8(1), 4 (1)	9 (3) 1), 1), 1), 1), 10, 10, 10, 10, 10, 10, 10, 10, 10, 10
15	1. 1. 1. (1H) (1H) (1H) (1H) (6H) (6H)	1. 1 -2. (2H (2H 6. 2 6-7	1. 1 (9H (2H (2H 5. 3	0.8 0.8 3.6 3.6 3.6 7.1
	1. 12(3H), 1. 15 (9H), 1. 80-2. 2 (2H), 3. 51(1H) 4. 15(2H), 5. 10 (1H), 6. 94(1H) 7. 58-7. 67(6H)	1. 10(3H), 1. 18(3H), 1. (9H), 2. 62-2. 96(2H), 3 (2H), 4. 12(2H), 4. 52(15, 74(1H), 6. 20-6. 35(21, 7. 56-7. 66(6H)	H), . 42	(H), 42 (H), (H), (H), (H), (H), (H), (H)
	2 (31)), 1.), 3. 5 (2), 6	0(3)), 4), 4 (1)	9(3)), 1), 4), 4), 4), 7.	0.85(3H) (3H), 1.4 (3H), 1.4 3.39(1H) (1H), 5.0 6.46(1H) 7.69(6H)
20	1.1 (9H) (2H) (2H) (1H) (1H)	1. 1 (9H (2H (2H 5. 7	1. 0 (3H) (1H) 5. 1	0.8 (3H) 3.33 3.3 (1H) (1H) (1H)
	9	9	Q	9
25	(0 0	S	တ အ	တ ဖာ
	Trt CtsHs3N3O9S amorphous	Trt C.+HsiNsOsS amorphous	4.0 HssN3OaS amorphous	4,Hs,N3OaS amorphous
	r ph	rph	rpl	Nrs N
30	s H s	+ H.	amo	H + + H ome
	J P	<u>ئ</u> "	ن ^{۱۷}	ن
	Trt	<u></u>	L-Ala-OEt Trt C.ellssN3OsS amorphous	L-Val-OMG Trt C17Hs7N3OsS amorphous
35)Et	9 7E 0
	Gly-0Et	Gly-OEt	a - (<u> </u>
	- X	11 y -	A-,	>
40	<u>G</u>			
	i	<u> </u>	د ا	
(PG	i			
45	08s1	0.082	-0B2	30
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000)	9-1	J)-7-)
50	Boc -1, -0 lu	- 50	Boc-L-Glu-0Bz1] 1 000
(pend	, 	D-8 Boc-L-Asp-0Bz1	}	D-10 Boc-L-Giu·OB:1
ر ا ع	7-0	D-8	D-9	-0

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5	0. 85(3H), 0. 88(3H), 1. 06(3H), 1. 15 (3H), 1. 39(9H), 1. 60-2. 37(5H), 3. 68(3H), 3. 76(1H), 4. 26(1H), 4. 44 (1H), 5. 07-5. 23(2H), 5. 37(1H), 6. 38 (1H), 6. 49(1H), 7. 15-7. 44(14H), 7. 56-7. 66(6H)	5. 85-0. 97(6H), 1. 10(3H), 1. 18(3H), 1. 22(3H), 1. 42(9H), 1. 30-2. 27(7H), 3. 61(1H), 4. 11(2H), 4. 34(1H), 4. 44 (1H), 5. 10(2H), 5. 40(1H), 6. 10(1H), 6. 39(1H), 7. 14-7. 40(14H), 7. 58-7. 67(6H)	1. 22(3H), 1. 26(3H), 1. 42(9H), 1. 67 -2. 34(8H), 3. 06-3. 20(1H), 3. 40- 3. 52(1H), 3. 63(3H), 3. 93(1H), 4. 37 (1H), 4. 42(1H), 5. 12(2H), 5. 36(1H), 6. 42(1H), 7. 10-7. 44(14H), 7. 49- 7. 72(6H)
10	8(3H), 1. 06), 1. 60-2. 3 6(1H), 4. 26 23(2H), 5. 3), 7. 15-7. 4	85-0.97(6H), 1.10(3H), 1.18(3H) 22(3H), 1.42(9H), 1.30-2.27(7H) 61(1H), 4.11(2H), 4.34(1H), 4.4.5.10(2H), 5.40(1H), 6.10(1H) 39(1H), 7.14-7.40(14H), 7.58-67(6H)	26(3H), 1. 4 . 06-3. 20(1 63(3H), 3. 9 H), 5. 12(2H) 10-7. 44(14
15	0. 85(3H), 0. 88(3H), 1. 06(3H), 1. 15 (3H), 1. 39(9H), 1. 60-2. 37(5H), 3. 68(3H), 3. 76(1H), 4. 26(1H), 4. 44 (1H), 5. 07-5. 23(2H), 5. 37(1H), 6. 3 (1H), 6. 49(1H), 7. 15-7. 44(14H), 7. 56-7. 66(6H)	85-0.97(6H), 1.10(3H), 1.18(3H), 22(3H), 1.42(9H), 1.30-2.27(7H), 61(1H), 4.11(2H), 4.34(1H), 4.44 (H), 5.10(2H), 5.40(1H), 6.10(1H), 39(1H), 7.14-7.40(14H), 7.58-67(6H)	1. 22(3H), 1. 26(3H), 1. 42(9H), 1. 6 -2. 34(8H), 3. 06-3. 20(1H), 3. 40- 3. 52(1H), 3. 63(3H), 3. 93(1H), 4. 3 (1H), 4. 42(1H), 5. 12(2H), 5. 36(1H) 6. 42(1H), 7. 10-7. 44(14H), 7. 49- 7. 72(6H)
20	(31) (31) (31) (11) (11) (11)	0. 0. 1. 1. 3. (1 (1 (1)) 1. (1) 1.	3. 2. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7.
	Φ	9	9
25	47Hs7NsO8S amorphous	C.5 Hei N3 Oe S m. p. 177.0-	C.7.HssN3O8S amorphous
30	C.7Hs7N3O8S amorphous	1	l I
		EL C	F
35	L-Val-OMe	L-Leu-OEt	L-Pro-0Et
40			
			_`
45	(continued)	1 - 08 z l	17 OB21
	()	Boc-16	Boc. L (
50	1 Boo	2 Bo	
	Table	D-12	D-13
55			

5 10	1. 08(3H), 1. 13(3H), 1. 26(3H), 1. 42 (9H), 1. 54-2. 24(4H), 3. 02(2H), 3. 39(1H), 4. 12(2H), 4. 32(1H), 4. 75 (1H), 5. 12(2H), 5. 46(1H), 6. 20- 6. 38(2H), 7. 03-7. 38(19H), 7. 53- 7. 63(6H)	0. 26(9H), 1. 09(3H), 1. 15(6H), 1. 43 (9H), 1. 58-2. 30(4H), 2. 95(2H), 3. 33 (1H), 4. 06(2H), 4. 33(1H), 4. 70(1H), 5. 12(2H), 5. 49(1H), 6. 23(1H), 6. 32 (1H), 6. 75(2H), 6. 97(2H), 7. 10-7. 40 (14H), 7. 55-7. 65(6H)	1. 08(3H), 1. 18(3H), 1. 22(3H), 1. 26 (3H), 1. 42(9H), 1. 80-2. 42(8H), 3. 49(1H), 4. 10(2H), 4. 12(2H), 4. 34 (1H), 4. 48(1H), 5. 11(2H), 5. 41(1H), 6. 30(1H), 6. 40(1H), 7. 15-7. 37 (14H), 7. 57-7. 69(6H)
20	6 (9H), 1.5 3.39(1H) (1H), 5.1 6.38(2H) 7.63(6H)	6 (9H) (1H) 5. 12 (1H) (1H)	6 (3H) 3. 49 (1H) (14H) (14H)
25	Trt Cs2Hs9N3O8S amorphous	CssHerNsOsSSi amorphous	Trt CsoHeiN3010S m.p.167.0-
30	ر پ پ		. E €
35	L-Phe-OEt Tr	SiMes L-Tyr-OEt Trt	L-Glu-OEt Tr
40			
S & S I (continued)	Boc-L-Glu-0Bz1	Boc-L-Glu-0Bzl	Boc-L-Glu OB::1
s Fable	D - 1 4	D-15	91-0

		. 68 . 28 0 -	(2)	H),
5		1. 07(3H), 1. 16(3H), 1. 41(9H), 1. 6 -2. 23(4H), 3. 89(1H), 4. 31(1H), 5. 10(2H), 5. 36(1H), 6. 09(1H), 6. 2 -6. 43(2H), 7. 10-7. 36(24H), 7. 50- 7. 58(6H)	07(3H), 1. 19(3H), 1. 41(9H), 70-2. 27(4H), 2. 72-3. 12(2H), 96(1H), 4. 32(1H), 4. 80(1H), 94-5. 22(6H), 5. 43(1H), 6. 25(1H), 52(1H), 7. 03-7. 44(24H), 56-7. 64(6H)	11(3H), 1. 21(3H), 1. 23(3H), 43(9H), 1. 72-2. 28(6H), 2. 05(3H), 47(2H), 3. 38(1H), 4. 15(2H), 34(1H), 4. 56(1H), 4. 97-5. 23(2H), 42(1H), 6. 25(1H), 6. 39(1H), 14-7. 37(14H), 7. 58-7. 67(6H)
10		16(3II), 1. . 89(1II), 4 36(1II), 6. . 10-7. 36(19(3H), 1. 12-3 32(1H), 4. H), 5. 43(1H), 4. H), 5. 43(1H), H)	21(3H), 1. 72-2. 28(8 38(1H), 4. 56(1H), 4. 25(1H), 6. 4H), 7. 58-
15		1. 07(3H), 1. 16(3H), 1. 41(9H), 1 -2. 23(4H), 3. 89(1H), 4. 31(1H), 5. 10(2H), 5. 36(1H), 6. 09(1H), 6. 09(1H), 6. 43(2H), 7. 10-7. 36(24H), 7. 57. 58(6H)	07(3H), 1.19(3H), 1.41(9H), 70-2.27(4H), 2.72-3.12(2H), 96(1H), 4.32(1H), 4.80(1H), 94-5.22(6H), 5.43(1H), 6.25(52(1H), 7.03-7.44(24H), 56-7.64(6H)	11(3H), 1. 21(3H), 1. 23(3H), 43(9H), 1. 72-2. 28(6H), 2. 05(47(2H), 3. 38(1H), 4. 15(2H), 34(1H), 4. 56(1H), 4. 97-5. 23(42(1H), 6. 25(1H), 6. 39(1H), 14-7. 37(14H), 7. 58-7. 67(6H)
20		12. 5. 5. 7. 7.		7. 5. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7.
		9	φ	
25		Cs.Hs.N.O.S amorphous	CsaHeaNaO.oS amorphous	C. B. H. 5 B. N. 3 O. B. S. 2 M. p. 161.5- 163.0
30		Cs + Hg amo	Cs s Hr	m. p.
		۳- ب	L. (tı tı
35	' :	MICHPh ₂	L-Asp-0Bz1	L-Met-OEt
40		_		
45 50	1 (continued)	Boc - L 61u · 01sz l	Boc-L-61u-()B21	Boc-L-Glu-0Bzl
	Table	D-17 B	D-18 B	D-19 B
	64			

	a a		
5	0. 76-0. 96(6H), 1. 00-1. 59(2H), 1. 11(3H), 1. 20(3H), 1. 43(9H), 1. 71-2. 30(5H), 3. 43(1H), 3. 65(3H), 4. 36(1H), 4. 44(1H), 4. 95-5. 22(2H), 5. 44(1H), 6. 28(1H), 6. 45(1H), 7. 08-7. 42(14H), 7. 52-7. 76(6H)	1. 00(3H), 1. 15(3H), 1. 36(9H), 1. 53-2. 26(4H), 3. 98(1H), 4. 03(1H), 5. 12(2H), 5. 33(1H), 6. 15(1H), 6. 56(1H), 6. 89(1H), 7. 08-7. 36(24 H), 7. 50-7. 58(6H)	0. 76-0. 90(6H)), 1. 09(3H), 1. 54(3H), 1. 22(3H), 1. 30-2. 32(7H), 1. 39(9H), 3. 67(1H), 4. 11(2H), 4. 24(1H), 4. 50(1H), 5. 14(2H), 5. 32(1H), 6. 30(1H), 6. 40(1H), 7. 14-7. 37(14H), 7. 55-7. 64(6H)
10	1), 1. 00-1 20(311), 1. 1), 3. 43(1 14(111), 4. 28(111), 6.	15(3H), 1. 1), 3. 98(1 33(1H), 6. 39(1H), 7. 3(6H)	(1), 1. 09(22(3H), 1. 57(1H), 4. 50(1H), 5. 80(1H), 6. HH), 7. 55-
15	0. 76-0. 96(6H), 1. 00-1. 59(2H), 1. 11(3H), 1. 20(3H), 1. 43(9H), 1. 71-2. 30(5H), 3. 43(1H), 3. 65(4, 36(1H), 4. 44(1H), 4. 95-5. 22(5, 44(1H), 6. 28(1H), 6. 45(1H), 7. 52-7. 76(6H), 7. 08-7. 42(14H), 7. 52-7. 76(6H)	1. 00(3H), 1. 15(3H), 1. 36(9H), 1. 53-2. 26(4H), 3. 98(1H), 4. 03 5. 12(2H), 5. 33(1H), 6. 15(1H), 6. 56(1H), 6. 89(1H), 7. 08-7. 36 H), 7. 50-7. 58(6H)	0. 76-0. 90(6H)), 1. 09(3H), 1. 54(3H), 1. 22(3H), 1. 30-2. 32(1. 39(9H), 3. 67(1H), 4. 11(2H), 4. 24(1H), 4. 50(1H), 5. 14(2H), 5. 32(1H), 6. 30(1H), 6. 40(1H), 7. 14-7. 37(14H), 7. 55-7. 64(6H)
20	1. 1. 2. 6. 7. 0. 7. 0. 7. 0	1. (1. § 5. J 6. § H),	6. 2
	ယ	9	ပ
25	C. e H.s.a.N.a.O.s.S m. p. 159.5- 160.5	Cs.Hs7NsOsS amorphous	Trt C.oHeiNaOeS amorphous
30	C + B }	Cs+H amc	C+oH
	← 1	ا ا ب	Tr
35	L-Ile-OMe Trt C+ # Hs o No O a S m. p. 159.5-	NHCHPh ₂	L-Leu-OEt
40		Q	Q
continued)	Roc-L-6fu 03x1	FBoc-L-Glu-0Bzl	Boc-L-Glu-0Bzl
Table	D-20 8	D-21 B	D-22 B
T T	Ö	<u> </u>	<u>-</u>

	(1H),	(1H),	(1H),
5	H), .62 H), H),	_	16(3H), H), 3. 48(00(1H), 11(2H), 58(1H), 7. 69(6H)
10	(6H), 1. 4 , 3. 03(2H), 4. 3 (1H), 4. 3 5-7. 40(1H)	9(6H), 1. 2-2. 42(8 2(2H), 4. 4(2H), 5. 1(1H), 7. (6H)	5(3H), 1. 0-2. 26(4 6(1H), 4. 4(1H), 5. 2(1H), 6. H), 7. 59-
15	1. 02(3H), 1. 12(6H), 1. 40(9H), 1. 60-2. 29(4H), 3. 03(2H), 3. 62(4H), 4. 06(2H), 4. 24(1H), 4. 73(1H), 5. 14(2H), 5. 36(1H), 6. 31(1H), 6. 54(1H), 7. 06-7. 40(19H), 7. 65-7. 64(6H)	1. 11(3H), 1. 19(6H), 1. 22(3H), 1. 39(9H), 1. 52-2. 42(8H), 3. 51(1H), 4. 03(2H), 4. 12(2H), 4. 24(1H), 4. 50(1H), 5. 14(2H), 5. 32(1H), 6. 31(1H), 6. 71(1H), 7. 14-7. 36(14), 7. 56-7. 65(6H)	0. 04(9H), 1. 15(3H), 1. 16(3H), 1. 42(9H), 1. 60-2. 26(4H), 3. 48(1H), 3. 65(3H), 3. 86(1H), 4. 00(1H), 4. 31(1H), 4. 54(1H), 5. 11(2H), 5. 40(1H), 6. 32(1H), 6. 58(1H), 7. 13-7. 35(14H), 7. 59-7. 69(6H)
20	1. 4. 6. 6	1. 1. 4. 6. (H)	0 1 8 4 10 1
	9	9	Φ
25	Cs2Hs9NsOeS amorphous	CsofferNsOroS amorphous	48H61N3O9SSi amorphous
30	Cs 2 Hs amor	CsoHe amoj	C48H6 amol
		Trt	T T
35	L-Phe-OEt	_0Et L-G1u-0Et	Si(Me)3 L-Ser-OMe Trt C. 8H6.1N3O3SSi amorphous
40	Q		د_
50 (Continued)	Boc-L-61u-	D-24 Boc-L-Glu-0Bz1	Boc-L-Glu-0Bz1
ָרַ ט. ה -3	D-23	D-24	D-25
-	· L		

5 10	0. 97(6H), 1. 39(9H), 1. 63-2. 50(8H), 3. 44-3. 68(1H), 3. 64(3H), 3. 71-3. 85 (1H), 4. 28(1H), 4. 42(1H), 4. 77(1H), 5. 15(2H), 5. 36(1H), 6. 39(1H), 7. 12- 7. 36(14H), 7. 50-7. 62(6H)	1. 08(3H), 1. 15(3H), 1. 17(3H), 1. 30 (3H), 1. 42(9H), 1. 63-2. 28(4H), 2. 97 (2H), 3. 39(1H), 4. 76(2H), 4. 27(2H), 4. 32(1H), 4. 59(2H), 4. 71(1H), 5. 12 (2H), 5. 46(1H), 6. 23(1H), 6. 31(1H), 6. 81(2H), 7. 03(2H), 7. 10-7. 42(14 H), 7. 54-7. 66(6H)	*0.72(3H), 0.80(3H), 0.94(12H), 1.22-2.40(20H), 1.36(9/2H), 1.37 (9/2H), 2.80-3.50(10H), 4.04(1H), 4.39(1H), 4.50(1H), 5.12(2H), 7.09-8.07(28H)
20	0.97(6H) 3.44-3.6 (1H),4.2 5.15(2H) 7.36(14H)	1. 08(3H) (3H), 1. 4 (2H), 3. 3 4. 32(1H) (2H), 5. 4 6. 81(2H) H), 7. 54-	*0.72(3H), 0.80 1.22-2.40(20H) (9/2H), 2.80-3. 4.39(1H), 4.50(7.09-8.07(28H)
	co.	CO	o
2 5 30	C+71155N3O8S amorphous	CseHesN3011S amorphous	CseHsoN+O.182 amorphous
	l e		T 1
35	L-Pro-OMe Trl	CH ₂ COOEt Tyr-OEt	SO3·Bu,N DL-Phe-OH
40	Ω	L	ت.
s s	Boc-L-Glu-0Bz1	Boc-L-Glu-0Bz1	Boc-L-Glu-0Bzl
Table	D-26	D-27	D-28

				~ ~
5	1. 09(3H), 1. 19(3H), 1. 27(3H), 1. 41 (9H), 2. 64-2. 93(2H), 3. 48(1H), 3. 94 (2H), 4. 17(2H), 4. 55(1H), 5. 12(2H), 5. 66(1H), 6. 14-6. 33(2H), 7. 10-7. 32 (14H), 7. 52-7. 64(6H)	1. 08(3H), 1. 18(3H), 1. 42(9H), 1. 83 2. 32(4H), 3. 63-3. 72(1H), 4. 34(1H), 5. 12(2H), 5. 39(1H), 6. 49(1H), 7. 10 -7. 43(15H), 7. 48-7. 56(6H)	1. 04(3H), 1. 06(3H), 1. 43(9H), 3. 73 (1H), 4. 00(2H), 5. 69(2H), 6. 68(1H) 7. 10-7. 33(9H), 7. 54-7. 64(6H), 8. 28(1H)	0. 97(6H), 1. 37(9H), 1. 80-2. 62(4H), 4. 18-4. 90(3H), 5. 69(1H), 6. 83(1H), 7. 12-7. 30(9H), 7. 46-7. 61(6H), 8. 06(1H)
10	(3II), 1. 27 3(2II), 3. 4 4. 55(1II) -6. 33(2II) 64(6II)	(3H), 1. 4 3-3. 72(1H 9(1H), 6. 4 48-7. 56(6(3H), 1. 4), 5. 69(2H)), 7. 54-7.	7(9H), 1.8), 5.69(1H)
15	1. 09(3H), 1. 19(3H), 1 (9H), 2. 64-2. 93(2H), (2H), 4. 17(2H), 4. 55(5. 66(1H), 6. 14-6. 33((14H), 7. 52-7. 64(6H)	1. 08(3H), 1. 18(3H), 1. 42(9 2. 32(4H), 3. 63-3. 72(1H), 4 5. 12(2H), 5. 39(1H), 6. 49(1 -7. 43(15H), 7. 48-7. 56(6H)	1.04(3H), 1.06(3H), 1.43(9H), 3 (1H), 4.00(2H), 5.69(2H), 6.68(7.10-7.33(9H), 7.54-7.64(6H), 8.28(1H)	97(6H), 1.37(9H), 1.80-2.62(18-4.90(3H), 5.69(1H), 6.83(12-7.30(9H), 7.46-7.61(6H), 06(1H)
20	1.09 (9H) (2H) 5.66 (14H	2. 32 2. 32 5. 12 -7. 4	1. 0. (1H.) 7. 10	4. 1 7. 1 8. 0
	9	co	-	-
25	soor soor	.H.eN20,S.amorphous	.HseN2OsS amorphous	+H+0N2O1S amorphous
30	C++Hs1N3OsS amorphous	C.1H.8N2O7S amorphou	C3.H3.6N2OsS amorphou	C3
		<u>L</u>	T 1	F -
35	G1y-0Et	НО	G 1 y OH	110
40			0	a
45	3			
45 45	1 1	-61u-0821		110. n.10-7
50	7-20	Boc-L-G	30 c	30c-L
{ - - -	D-29 Bc	D-30		E - 2

			71	76
5	(2-2.53 68(1H), (), 7.49-	7(3H), 1(1H),), 7.54-	5(9H), 1. H), 4. 20-), 7. 06-), 8. 05-	9(9H), 1. H), 6.64
10	6(911), 1. 8 85(314), 5. 3-7. 32(911) 9(111)	1(3H), 1. 9 7(2H), 6. 5 2-7. 38(9H)	7(3H), 1. 4 17-3. 70(2 1-5. 50(2H	5(3H), 1. 3 56-4. 34(4 .6(19H)
15	0. 96(6H), 1. 36(9H), 1. 82-2. 53 (4H), 4. 20-4. 85(3H), 5. 68(1H), 6. 81(1H), 7. 13-7. 32(9H), 7. 49- 7. 63(6H), 8. 09(1H)	1. 08(3H), 1. 11(3H), 1. 97(3H), 3. 89(1H), 3. 97(2H), 6. 51(1H), 6. 62(1H), 7. 12-7. 38(9H), 7. 54- 7. 67(6H), 7. 00-8. 00(1H)	0.89(3H), 0.97(3H), 1.45(9H), 1.71 -2.80(4H), 3.47-3.70(2H), 4.20- 4.73(2H), 5.07-5.50(2H), 7.06- 7.27(9H), 7.47-7.64(6H), 8.05- 9.00(3H)	1. 05(3H), 1. 06(3H), 1. 39(9H), 1. 76 -2. 56(4H), 3. 66-4. 34(4H), 6. 64 (1H), 6. 00-8. 16(19H)
20	0. 9(411) (411) 6. 81	1. 08 3. 89 6. 62 7. 67	0.89 -2.8 4.73 7.27 9.00	1.05 -2.5 (1H)
	<u></u>		t	
25	C3+H+0N2O7S amorphous	C28H30N2O4S amorphous.	3.6H+3N3O8S amorphous	amorphous
30	C3		0	Csell+sNsOsS amorphous
	Trt	- r	Tr t	
35	HO	G 1 y - O [[Gly-0H	G1y-OH
40		G	G1	G
				Ω
tinued)	110 - 130 - 130		n -011	HO-n
s l (continu	30c-D-G(a+0)	A C	Boc-L-Glu-01	Boc-L-Glu-OH
rable Table	- 3 - 3	다 구	ය - ස	E - 3
55 E			ω	Сī

5	5(9H), 80(2H), 52(2H), 68(6H),	38(9H), 40(2H), 1), 4.07 88(16H), 28(1H)	34(9H), .70(4H), .1H), 7.44	. 26(3H), H), 3. 33 H), 4. 53 7. 49-7. 59 H), 12. 20
10	(31;), 0. 96(31!), 1. 45(91!) -2. 76(41!), 3. 44-3. 80(21:4.70(21!), 5. 10-5. 52(21:4.7. 36(91!), 7. 44-7. 68(61:4.7. 45(31!))	81(3H), 1.), 2. 15-2. 8-3. 89(2H), 6. 80-7. 2(1H), 12.	6(3H), 1. 3), 3. 60-4. 0-7. 30(1) 54(2H)	82(3H), 1, 10-2, 54(4), 4, 15(1), 8, 38(1), 8, 38(1)
15	1. 89(3H), 0. 96(3H), 1. 45(9H), 1. 70-2. 76(4H), 3. 44-3. 80(2H), 1. 20-4. 70(2H), 5. 10-5. 52(2H), 7. 02-7. 36(9H), 7. 44-7. 68(6H), 7. 90-9. 45(3H)	*0.77(3H), 0.81(3H), 1.38(9H), 1.65-2.10(2H), 2.15-2.40(2H), 3.34(1H), 3.58-3.89(2H), 4.07 (1H), 4.40(1H), 6.80-7.88(16H), 7.77(1H), 8.42(1H), 12.28(1H)	0. 98(3H), 1. 06(3H), 1. 34(9H), 2. 64-3. 08(2H), 3. 60-4. 70(4H), 5. 90(1H), 6. 90-7. 30(11H), 7. 44 -7. 66(6H), 9. 54(2H)	*0. 78(3H), 0. 82(3H), 1. 26(3H), 1. 39(9H), 1. 60-2. 54(4H), 3. 33 (1H), 3. 93(1H), 4. 15(1H), 4. 53 (1H), 7. 04-7. 38(10H), 7. 49-7. 59 (6H), 8. 11(1H), 8. 38(1H), 12. 20 (1H)
20	1. 7 4 . 2 7 . 0 7 . 0 7 . 0	*0. 1. 6 3. 8 7. 7	2. 2. 5. – 7. – 7.	* 1 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	L	7		
25	CoeHtoNoOeS amorphous	CieH+iNiOsS amorphous	C35H41N3O8S amorphous	Ca7H+5NaOaS amorphous
30	1	ت		
	Trt	٦.	[— 1-4	±2 ∐ [→
35	G i y -011	G 1 y - OH	Gly-0H	L-Ala-OH
40	Ω	_1	۵	
45	30c-D-61u-(Boc-L-Glu-	Boc-L-Asp-OH	Boc-L-Glu-Off
ا د ح ر	2 CT	H) -00	හ - ස	E-10

	5 0	45	40	35		30	25	20	15	10	5
Table	Table 1 (continued)	inued)				,					
								0.86(3H), 0.89(3H), 1.02(3H),). 89(3H),	1.02(3H),	
E-11	E-11 Boc-L-Glu-OH	110-		L-Val-011	Trt	L-Val-OII Trt Cos II+ 3 N3 O8 S		1.06(3H),	41(9H),	[.06(3H), [.4](9H), [.80-2.55	
						amorphous		(5H), 4. Ub(1H), 4. 24.	(5H), 4. Ub(1H), 4. Z4-4. 40(ZH), E. E9(TH) 7. A7-7. 23(TH) 7. 43	
								(1H), 7. 53-7. 65(6H), 8. 50(2H)	-7.65(6H)	, 8. 50(2H)	
		-						0.87(3H),	0.90(3H),	0.87(3H), 0.90(3H), 1.04(3H), 1.08	80
7 - 1	F-19 Roc-1,-G1u-01	110-	_	L-Val-OH	Trt	Trt CasHasNaOsS	7	(3H), 1. 41	(911), 1.81	(3H), 1. 41(9H), 1. 81-2. 57(5H),	
1		;				amorphous		4.07(1H),	1, 25-4, 50	4.07(1H), 4.25-4.50(2H), 5.69(1H),	[H),
								7.03-7.30	(10H), 7.4	7.03-7.30(10H), 7.40(1H), 7.51-	
	··· -							7.66(6H), 8.52(2H)	8. 52(2H)		
	Į.							*0.77-0.9	0(6H), 0.8	*0.77-0.90(6H), 0.87(3H), 0.90	
1 1 2	R-13 ROC-1-0-11-0H	110-		L-Leu-OH	Trt	Trt C.o.Hs.1N3O8S	<u></u>	(3H), 1.39	(9H), 1.30	(3H), 1. 39(9H), 1. 30-2. 12(5H),	
7 7		:	1			amorphous		2.36(2H),	3.68(1H),	2.36(2H), 3.68(1H), 3.94(1H), 4.22	22
								(111), 4.49	(1H), 7.08	(1H), 4. 49(1H), 7. 08-7. 35(10H),	
								7,50-7.62	(6H), 8.07	7, 50-7, 62(6H), 8, 07(1H), 8, 18(1H),	1H),
								12.32(1H)			
								*0,96(3H)	, 1. 12(3H)	*0, 96(3H), 1. 12(3H), 1. 37(9H),	
(1 (1	10-11-0-1-0-1	110-1		L-Pro-OH		Trt C39H+7N3O8S	7	1.57-2.52	(8H), 3.06	1.57-2,52(8H), 3.06-3.62(3H),	,
1	2	:	i			amorphous	·	3.93(1H),	4.14(1H),	3.93(1H), 4.14(1H), 4.27(1H), 7.09	60.
						4		(1H), 7.10	-7.38(9H)	(1H), 7.10-7.38(9H), 7.44-7.62	
								(6H), 8.10	(6H), 8. 10(1H), 12. 40(1H)	10(1H)	
		T									

	50	45	40	35		30	25	20	15	10	5
rable	1 (contin	inued)						-	0 (110)01	06 1 (116)0	(10)
E-13	Boc-L-G	IIO-n1		L-Phe-OH	Trt	C.3H.8N.O.S amorphous	sno!	7	*0.72(3H), 0.79(3H), 1.39(3H), 1.66-2.12(2H), 2.20-2.36(2H), 2.79-3.12(2H), 3.84-4.05(1H),	9(3H), 1. 35 , 2. 20-2. 36 , 3. 84-4. 05	(2H), 5(1H),
									4. 42(1H), 4. 47(1H), 7. 05-7. 34 (15H), 7. 48-7. 60(6H), 7. 97(1H), 8. 32(1H), 12. 50(2H)	60(6H), 7.9 60(6H), 7.9 0(2H)	37(1H),
т	Boc-L-61	In -0!!		L-Tyr-0H	T r.	Trt C.sH.sNsOsS amorphous	.008S	<u></u>	1. 00(6H), 1. 43(9H), 1. 80-2. 50(4H), 2. 77-3. 17(2H), 3. 84(1H), 4. 26(1H), 4. 70(1H), 5. 74(1H), 6. 57(1H), 6. 71 (2H), 6. 83(1H), 6. 94(2H), 7. 09-7. 38 (9H), 7. 53-7. 63(6H), 6. 50-9. 90(3H)	(9H), 1.80 (3.84(1H), (1H), 6.57 (6.94(2H)), (6.553(6H), 6.55	-2.50(4H), ,4.26(1H), (1H),6.71 ,7.09-7.38 0-9.90(3H)
:: 	Boc-1,-61u-	110-n		L-Glu-0H	14 14 (CasH47N3O10S amorphous	So.0s		0. 99(3H), 1. 09(3H), 1. 43(9H), 1. 85- 2. 64(8H), 3. 91(1H), 4. 23(1H), 4. 49 (1H), 5. 81(1H), 6. 98(1H), 7. 10-7. 43 (10H), 7. 52-7. 74(6H), 8. 20-11. 6 (3H)	9(3H), 1. 43 1(1H), 4. 23), 6. 98(1H) . 74(6H), 8.	(9H), 1.85- (1H), 4.49 , 7.10-7.43 20-11.6
⊕ 11 8	Boc-L-Glu-	JIO-n1		NHCHPh2	F-	Trt C., Hs. N.O.s S amorphous	30.s hous	_	1. 06(6H), 1. 40(9H), 1. 70-2. 50(4H), 4. 12(1H), 4. 26(1H), 5. 48(1H), 6. 06 (1H), 6. 61(1H), 6. 94-7. 34(20H), 7. 46-7. 55(6H), 6. 90-8. 00(1H)	0(9H), 1. 7(6(1H), 5. 48), 6. 94-7. 7), 6. 90-8.	3(1H), 6.06 34(20H), 34(20H),

5 5	50	45		35 40		30	25	20	20	15	10	5
Table	 4	(continued)										
E - C	Boc - L - G u - O	0.		L-Asp-011		Coeff+5NoOloS amorphous	Sos		*0.79(3H) 1.60-2.78 4.40-4.58 7.49-7.60 12.51(2H)	H), 0. 82(78(6H), 358(2H), 760(6H), 8	*0.79(3H), 0.82(3H), 1.39(9H), 1.60-2.78(6H), 3.36(1H), 3.95(1 4.40-4.58(2H), 7.08-7.38(10H), 7.49-7.60(6H), 8.11(1H), 8.37(1 12.51(2H)	*0.79(3H), 0.82(3H), 1.39(9H), 1.60-2.78(6H), 3.36(1H), 3.95(1H), 4.40-4.58(2H), 7.08-7.38(10H), 7.49-7.60(6H), 8.11(1H), 8.37(1H), 12.51(2H)
E-20	Boc-L-Glu-0	n -0][ے	L-Met-OH	7 7	CasHtsN;0sSz amorphous	S ₂		*0.78(3 -2.60(8 (1H), 4. (10H), 7 8.30(1H	*0.78(3H), 0.82(3H) -2.60(8H), 2.00(3H) (1H), 4.28(1H), 4.50 (10H), 7.50-7.60(6H) 8.30(1H), 12.52(1H)	*0.78(3H), 0.82(3H), 1.38(9H), 1. -2.60(8H), 2.00(3H), 3.33(1H), 3. (1H), 4.28(1H), 4.50(1H), 7.10 ² 7. (10H), 7.50-7.60(6H), 8.10(1H), 8.30(1H), 12.52(1H)	*0.78(3H), 0.82(3H), 1.38(9H), 1.64 -2.60(8H), 2.00(3H), 3.33(1H), 3.95 (1H), 4.28(1H), 4.50(1H), 7.10-7.36 (10H), 7.50-7.60(6H), 8.10(1H), 8.30(1H), 12.52(1H)
E-21	Boc-L-Glu-0II	n-0il	ы	L-11e-0H	Trt	CtoHsiN3O8S amorphous	ω _w	-	*0.70-0 1.38(9H (2H),3. 4.54(1H) 7.60(6H) (1H)	90(12H)), 1. 66-2 32(1H), 3), 7. 11-7), 8. 00(1	*0.70-0.90(12H), 1.02-1.54(2H), 1.38(9H), 1.66-2.10(3H), 2.22-2. (2H), 3.32(1H), 3.93(1H), 4.11(1H), 4.54(1H), 7.11-7.37(10H), 7.48- 7.60(6H), 8.00(1H), 8.08(1H), 12. (1H)	*0.70-0.90(12H), 1.02-1.54(2H), 1.38(9H), 1.66-2.10(3H), 2.22-2.42 (2H), 3.32(1H), 3.93(1H), 4.11(1H), 4.54(1H), 7.11-7.37(10H), 7.48- 7.60(6H), 8.00(1H), 8.08(1H), 12.42 (1H)
						1						

	50	45	40	35		30	25	20	15	10	5	
Tabl	e 1 (continu	cinued)										
E-22	Boc -L-G1u-0II	110-1	Q	NII CII Ph 2	<u>.</u>	С ₄₇ Н ₅₁ N ₃ O ₈ S m. p. 125.5- 127.0	ς, _α -		1, 05(3H), 1 1, 67-2, 38(5, 46(1H), 6 7, 00-7, 30(1. 05(3H), 1. 15(3H), 1. 38(9H), 1. 67-2. 38(4H), 3. 90(1H), 4. 01(1H), 5. 46(1H), 6. 13(1H), 6. 84(1H), 7. 00-7. 30(21H), 7. 46-7. 58(6H)	38(9H), 1), 4. 01(1H), 84(1H), 7. 58(6H)	
E - 2 3	Boc-L-Glu-0	10-	۵	L-Leu-OH	1	C+oHsiN3O8S amorphous	S n	7	*0.63-0.92 1.38(9H), 2 3.88(1H), 4 7.04(1H), 7 (6H), 8.14(*0.63-0.92(12H), 1.25-2.03(5H), 1.38(9H), 2.14-2.56(2H), 3.34(1H), 3.88(1H), 4.22(1H), 4.54(1H), 7.04(1H), 7.15-7.36(9H), 7.47-7.59 (6H), 8.14(1H), 8.42(1H), 12.44 (1H)	-2. 03(5H), H), 3. 34(1H), 54(1H), H), 7. 47=7. 59	
E - 24	Boc-L-G	11 O- n	Ω	L-Phe-OH	H (-	C+3H+9N3O8S amorphous	Sa	7	*0.59(6H), , 2.20-2.55 3.37(1H), 3 7.06-7.37(8.02(1H), 8	*0.59(6H), 1.39(9H), 1.78-2.10(2H), 2.20-2.55(2H), 2.79-3.11(2H), 3.37(1H), 3.94(1H), 4.31-4.51(2H), 7.06-7.37(15H), 7.43-7.56(6H), 8.02(1H), 8.37(1H), 12.60(1H)	3.11(2H), 3.11(2H), 31-4.51(2H), 7.56(6H), 60(1H)	
						1						

55	50	45	40	35		25 30		15 20	10	5
Table	 1	(continued)	ر ت							
6 - 25	Boc - L - G	10-n10	Q	L-G1u-OH	Trt	CasH+7NaO10S amorphous	1	*0.74(3H) 1.62-2.08 3.35(1H), (1H), 7.04 7.47-7.60 12.34(2H)	*0.74(3H), 0.80(3H), 1.39(9H), 1.62-2.08(4H), 2.12-2.54(4H), 3.35(1H), 3.88(1H), 4.24(1H), 4 (1H), 7.04(1H), 7.11-7.37(9H), 7.47-7.60(6H), 8.02(1H), 8.46(*0.74(3H), 0.80(3H), 1.39(9H), 1.62-2.08(4H), 2.12-2.54(4H), 3.35(1H), 3.88(1H), 4.24(1H), 4.53 (1H), 7.04(1H), 7.11-7.37(9H), 7.47-7.60(6H), 8.02(1H), 8.46(1H), 12.34(2H)
E-26	Boc-L-Glu-Off	J u - OH		L-Ser-OH	(7	C37H45N3O9S amorphous	7	*0.80(3H 1.62-2.1 3.34(2H) 3.93(1H) 7.06-7.3 8.10(1H)	*0.80(3H), 0.85(3H), 1.39(9H), 1.62-2.12(2H), 2.22-2.53(2H), 3.34(2H), 3.56-3.77(2H), 3.93(1H), 4.24(1H), 4.54(1H), 7.06-7.35(10H), 7.48-7.61(6H), 8.10(1H), 8.19(1H), 12.44(1H)	1.39(9H), 2.53(2H); 2H), .54(1H), -7.61(6H), 2.44(1H)
E-27	Boc - L -G l u · Oll	II 0 · n I :	Q	L-Pro-OH	Trt	Trt CasH47NaOaS amorphous	7	*0.85(3H 1.65-2.4 (2H), 3.7 4.80(1H) 7.43-7.5	*0.85(3H), 0.88(3H), 1.38(9H), 1.65-2.46(8H), 3.33(1H), 3.30- (2H), 3.75-3.97(1H), 4.20(1H), 4.80(1H), 6.99(1H), 7.14-7.17(7.43-7.55(6H), 8.17(1H), 12.42	*0.85(3H), 0.88(3H), 1.38(9H), 1.65-2.46(8H), 3.33(1H), 3.30-3.70 (2H), 3.75-3.97(1H), 4.20(1H), 4.80(1H), 6.99(1H), 7.14-7.17(9H), 7.43-7.55(6H), 8.17(1H), 12.42(1H)

55	50	45		35 40		30	25		15	10	5
Table	~	(continued)	1)		1.						
E-28	Boc-L-Glu-0	01u-01l		СН ₂ СООН Туг-ОН	F1 +1	C+sHsiNaOiiS amorphous	Suo	2	*0.75(3H), 1.60-2.14 2.75-3.02 4.37(1H), (2H), 7.04 (6H), 8.03	*0.75(3H), 0.81(3H), 1.39(9H), 1.60-2.14(2H), 2.21-2.46(2H), 2.75-3.02(2H), 3.35(1H), 3.98(1 4.37(1H), 4.48(1H), 4.60(2H), 6. (2H), 7.04-7.38(12H), 7.50-7.62 (6H), 8.03(1H), 8.27(1H), 12.67(*0.75(3H), 0.81(3H), 1.39(9H), 1.60-2.14(2H), 2.21-2.46(2H), 2.75-3.02(2H), 3.35(1H), 3.98(1H), 4.37(1H), 4.48(1H), 4.60(2H), 6.75 (2H), 7.04-7.38(12H), 7.50-7.62 (6H), 8.03(1H), 8.27(1H), 12.67(2H)
ਨ 2 1 2 3	Boc-L-G	J 0 10		SO3-Bu,N DL-Phe-OH	N Tr	CssHa+N+O11Sz amorphous	01.82 ous	-	*0.76(3H), 1.20-1.42(8H),1.72 (8H),1.72 ,2.80-3.3(1H),4.49(7.43-7.66(1H)),12.45(1H),	*0.76(3H), 0.82(3H), 0.94(12H), 1.20-1.42(8H), 1.38(9H), 1.47=1 (8H), 1.72-2.15(2H), 2.20-2.41(.2.80-3.30(11H), 3.94(1H), 4.41 (1H), 4.49(1H), 7.07-7.38(11H), 7.43-7.66(9H), 8.04(1H), 8.28(11 12.45(1H),	*0.76(3H), 0.82(3H), 0.94(12H), 1.20-1.42(8H), 1.38(9H), 1.47 ⁻¹ .68 (8H), 1.72-2.15(2H), 2.20-2.41(2H), 2.80-3.30(11H), 3.94(1H), 4.41 (1H), 4.49(1H), 7.07-7.38(11H), 7.43-7.66(9H), 8.04(1H), 8.28(1H), 12.45(1H),
H - 30	Boc - L - 2	() - d s\		G1y-011	(—	CosH41NoOmS amorphous	SaC ous		1. 12(3H), 1 2. 62-3. 05(4. 51(1H), 8 (11H), 7. 53	1. 12(3H), 1. 15(3H), 1. 28(9H), 2. 62-3. 05(2H), 3. 72-4. 32(3H), 4. 51(1H), 5. 93(1H), 6. 38-7. 39 (11H), 7. 53-7. 64(6H), 9. 63(2H)	28(9H), .32(3H), 38-7.39 9.63(2H)

55	50	45	40	35		25 30		10	
Table		(continued)							1
E-31	 Boc-L-Glu	110	_1	110	Trt	Trt CatlltoN207S	_	*0.85(3H), 0.89(3H), 1.38(9H), 1.62-2.11(2H), 2.23-2.38(2H),	
						amorphous	 	3. 40(1H), 3. 91(1H), 4. 11(1H), 7. 03(1H), 7. 14-7. 36(9H), 7. 47-7. 57 (6H), 8. 03(1H), 12. 52(1H)	
E-32	Boc			Gly-0H	Trt	C31H36N2O5S2	<u></u>	1. 04(3H), 1. 06(3H), 1. 43(9H)	
						amorphous		3.74(1H), 4.00(2H), 5.63(1H),	
								6. 65(1H), 7. 10-7. 35(9H), 7. 53-7. 61	
								(6H), 8.63(1H)	
F-1		[a	G I y -011	Ħ	C, H, + N2O3S.HCQ	∞	**1. 42(3H), 1. 49(3H), 3. 98(2H),	
						49-54° decomp.		3.99(1H)	
	L							**1. 38(3H), 1. 43(3H), 2. 01-2. 22	
F-2	H-L-Glu-OH		Q	НО	==	CIOHIBN2OSS·HCQ	∞	(2H), 2. 45-2. 59(2H), 3. 93(1H), 4. 43	5
						84-89° decomp.		(1H)	
	l							**1.37(3H), 1.42(3H), 2.08-2.22	
F-3	H-D-G1n-OH		Q	HO	=	C.oH.BN2O5S.HCQ	∞	(2H), 2.49-2.60(2H), 3.97(1H),	
						89-93° decomp.		4.41(1H)	
							,		
		1							1

	50	45	40	35		25	20	15	10	5	
Table	e 1 (contin	tinued)			i.						
P-4	Ac.	i		G1y-011	Ħ	CoHiBN2OtS 8	** 1.35	**1. 35(3H), 1. 42(3H), 2. 01(3H),	(311), 2.0	1(3H),	
						65-727decomp.	3.94(2	3.94(2H), 4.37(1H)	H)		
	L						**1.35	**1. 35(3H), 1. 41(3H), 2. 06-2.	(3H), 2.0	6-2.21	
F-5	11-L-G i u-01			G 1 y -0H	==	C. 2 H 2 1 N 3 O 8 S • H C Q 8	(2H), 2	(2H), 2. 41-2. 69(2H), 3. 93(2H), 3.	2H), 3.93	(2H), 3, 97	
						121-125Cdecomp.	(1H), 4	(1H), 4.38(1H)			
	L						**1.37	**1. 37(3H), 1. 42(3H), 2. 03-2.	(3H), 2.0	3-2.23	
F-6	H-L-G1u-OH	H	Ω	G1y-0H	==	C12H21N3O8S.HC@ 8	(2H), 2	(2H), 2. 43-2. 60(2H), 3. 94(3H)	2H), 3.94	(3H),	
						113-1170	4.41(1H)	H)		• •	
	,					decomb.					
							**1.35	**1. 35(3H), 1. 41(3H), 2. 07-2.	(3H), 2.0	7-2.21	
F-7	H-D-G]u-OH	H(Ω	G1y-0H	=	C12H21N3O8S.HCQ 8	(2H), 2	(2H), 2.41-2.67(2H), 3.93(2H),	2H), 3.93	(2H),	
					.	127-131°C	3.96(1	3.96(1H), 4.38(1H)	(H)		
						decomb.					
							**1.37	**1, 37(3H), 1, 42(3H), 2, 04	(3H), 2.0	4-2.27	
F-8	H-L-61u-			Gly-0H	Ħ	C12H21N3O6S.HCg 8	(2H), 2	(2H), 2.40-2.54(2H), 3.94(2H), 4.	2H), 3.94	(2H), 4.18	
						129-1351 decomp.	(1H), 4	(1H), 4.47(1H)			
	I	<u> </u>					**1.35	**1.35(3H), 1.40(3H), 2.89-3.	(3H), 2.8	9-3.17	
િ - 9	110-dsv 7-11	=		G1y-0H	==	CIIHIBN3O6S.HCQ 8	(2H), 3	(2H), 3.92(2H), 4.26(1H), 4.39(1H)	.26(1H),	4.39(1H)	
						130-134°Cdecomp.					

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40	
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55	

Table	1 (continued)					
0 1 - 4	F-10 H-L-Glu-011		L-Ala-OH	=	C13H2+N3O6S·HC2 8 125-128°C decomp.	**I. 35(6H), I. 40(3H), 2. 06-2. 21 (2H), 2. 40-2. 66(2H); 3. 97(1H), 4. 28 (1H), 4. 37(1H)
	H-L-Glu-011		L-Val-OH	=	C.sH27N3OsS.HCQ 8 128-133T decomp.	**0.87(3H), 0.90(3H), 1.36(3H), 1.40 (3H), 1.98-2.30(3H), 2.38-2.70(2H), 3.98(1H), 4.13-4.23(1H), 4.46(1H)
F - 1.2	H-L-Glu-0H	۵	L-Val-OH	H	C.sH27N3OsS.HC@ 8 119-124T decomp.	**0.89(3H), 0.92(3H), 1.34(3H), 1.39 (3H), 1.96-2.31(3H), 2.42-2.61(2H), 3.95(1H), 4.07-4.20(1H), 4.92(1H)
F - 13	II-F-01a-0II		L-Leu-OH	ш	C ₁₈ H ₂₉ N ₃ O ₈ S·HC _Q 8 114-119°C decomp.	**0. 78(3H), 0. 84(3H), 1. 35(3H), 1. 40(3H), 1. 53-1. 72(3H), 2. 03-2. 17 (2H), 2. 46-2. 58(2H), 3. 92(1H), 4. 34 (1H), 4. 38(1H)
(-)	F-14 II-L-Glu-OII		L-Pro-OH	æ	C15H25N3O6S.HCQ 8 148-152T decomp.	**1. 39(3H), 1. 41(3H), 1. 86-2. 67 (8H), 3. 80(2H), 3. 97(1H), 4. 35(1H) 4. 60-4. 80(1H)

	50	4 5	40	35		30	25	20	15	5		
able	l (continu	inued)										
	l							*	**1. 24(311), 1. 26(3H), 1. 96	3H), 1.96-2.2	4	
	- - -			L-Phe-OII	==	CigH27	C. 9 H 2 7 N 3 O 6 S - H C 2 8		(2H), 2. 28-2. 58(2H), 2. 82-3. 29(2H),	H), 2.82-3.29	(2H),	
,						119-125°C	<u></u>		3.97(1H), 4.30(1H), 4.69(1H),), 4.69(1H),		
						decomb.	.dm		7.13-7.32(511)			
	L								**1. 24(3H), 1. 26(3H), 1. 98-2. 24	3H), 1. 98-2. 8	4	
91-	- 1 - 0 n - 0			L-Tyr-OH	=	CioH271	C, 9 H 2 7 N 3 O 7 S • H C Q 8		(2H), 2. 29-2. 61(2H), 2. 74-3. 26(2H),	H), 2.74-3.26	(2H),	
						133-139°			3.94(1H), 4.30(1H), 4.69(1H), 6.72), 4.69(1H), 6	. 72	
						decomb	.dm	_	(2H), 7.05(2H)			
	L						*	*	. 38(3H), 1. 42(3H), 1. 83-2. 30(4H)	, 1.83-2.30(4	(H	
7-17	-L-C1n-0	1	ب	L-G1u-0H	==	CisHzsi	C15H25N3O+S-HCQ 8		2.39-2.65(4H), 3.95(1H), 4.40(1H),	95(1H), 4.400	[1H),	
						140-150°C	ຸວຸດ		4.42(1H)			
	***					de	ecomp.					
									*1. 29(3H), 1. 33(3H), 1. 85-2. 67(2H),	H), 1.85-2.6	(2H),	
ਜ - 1 ∞	H-F-C1n-OH	=		NHCHPh2	==	CzaHza	C23H29N3O4S.HCQ 8		3.40(1H), 3.86(1H), 4.70(1H), 6.12	(), 4, 70(1H),	3. 12	
						140-147C	J.		(1H), 7. 12-7. 43(10H), 8. 20(1H),	OH), 8. 20(1H)		
						Ϋ́	decomp.		8.50(1H), 9.13(1H)			
						!		-	**1. 39(3H), 1. 44(3H), 2. 10-2. 23	(3H), 2. 10-2.	23	
6 1 1	-12-01	=	IJ	L-Asp-OH	×	C1+H221	C1+H22N3O8S+HC2 8		(2H), 2. 51-2. 62(2H), 2. 94(2H), 3. 97	(H), 2. 94(2H)	3.97	
						128-1330	30		(1H), 4.41(1H)			
						· de(-decomb.					
		-										

		00	96 H),	55), H),	E),
5		**1.39(3H), 1.44(3H), 1.93-2.28 (4H), 2.04(3H), 2.41-2.70(4H), 4.00 (1H), 4.40(1H), 4.54(1H)	**0.83(3H), 0.89(3H), 1.05-1.56 (2H), 1.38(3H), 1.42(3H), 1.76-1.96 (1H), 2.06-2.30(2H), 2.43-2.72(2H), 4.01(1H), 4.25(1H), 4.47(1H)	*1.30(3H), 1.35(3H), 1.96-2.15 (2H), 2.36-2.57(2H), 2.80(1H), 3.55 (2H), 3.85(1H), 4.72(1H), 6.14(1H), 7.12-7.48(10H), 8.19(1H), 8.49(2H), 9.12(1H)	**0.70-0.79(6H), 1.36(3H), 1.41 (3H), 1.50-1.82(3H), 2.06-2.31(2H), 2.42-2.68(2H), 4.01(1H), 4.33(1H), 4.43(1H)
10		. 44(3H),), 2. 41-2.), 4. 54(1)	. 89(3H),), 1. 42(3H), 2. 30(2H), 2. 5(1H), 4.	35(3H), 1. 57(2H), 2.), 4.72(11) H), 8.19(6H), 1.36 82(3H), 2.), 4.01(1H)
15		**1.39(3H), 1.44(3H), 1. (4H), 2.04(3H), 2.41-2.7 (1H), 4.40(1H), 4.54(1H)	**0.83(3H), 0.89(3H), 1.05-1 (2H), 1.38(3H), 1.42(3H), 1.7 (1H), 2.05-2.30(2H), 2.43-2. 4.01(1H), 4.25(1H), 4.47(1H)	*1.30(3H), 1.35(3H), 1.96-2.15 (2H), 2.36-2.57(2H), 2.80(1H), (2H), 3.85(1H), 4.72(1H), 6.14(7.12-7.48(10H), 8.19(1H), 8.49 9.12(1H)	**0.70-0.79(3H), 1.50-1. 2.42-2.68(2H) 4.43(1H)
20		** 1 (4H)	**0. (2H) (1H) 4.0	*1. (2H) (2H) (2H) 7. 12 9. 12	**0. (3H) 2. 42 4. 43
		∞ .	∞	∞	∞
25		C.sHzeNaOeSz• HCQ 115-119°Cdecomp	C.eH29N3O6S.HC@ 121-126U decomp.	C23H29N3O4S.HC@ 120-125℃ decomp.	C.eH2sNaOeS·HCQ 125-129°C decomp.
30		C15H26 HC2 115-11	CieHz9N3(121-126C deco	C23H29N3(120-125℃ deco	C. 8 H 2 9 N 3 1 2 5 - 1 2 9 U
		н	==	=	Ħ
35		L-Met-OH	L-11e-0H	NIICHPh 2	L-Leu-OH
40				Q	Q
	=				
45	(continued)	H0-	110-	II (1 - 1) II	JIO-
5 <i>0</i>		H0-n1D-7-H	H-L-Glu-0		ال-1-1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1
55	Table	F-20	F - 21	F-22	F-23

	50	45	40	35		30		20	15	10	5
able	l (continu	inued)									
F - 24	II-L-G1u-0!!		۵	L-Phe-OH	==	C.9 H27N3OsS·HC2 126-129°C decomp.	нсд 8	*1.13(3 2.41-2. (2H), 3. 4.51(1H 8.20-8.	*1.13(3H), 1.18(3H), 1.90-2.13(2H) 2.41-2.66(2H), 2.58(1H), 2.41-2.58 (2H), 3.60(1H), 3.86(1H), 3.45(1H), 4.51(1H), 7.11-7, 40(5H), 8.12(1H), 8.20-8.80(3H), 12.50(1H)	3H), 1. 90 58(1H), 86(1H), 40(5H), 2. 50(1H)	*1. 13(3H), 1. 18(3H), 1. 90-2. 13(2H), 2. 41-2. 66(2H), 2. 58(1H), 2. 41-2. 58 (2H), 3. 60(1H), 3. 86(1H), 3. 45(1H), 4. 51(1H), 7. 11-7, 40(5H), 8. 12(1H), 8. 20-8. 80(3H), 12. 50(1H)
F - 25	H-L-Glu-011	=	Q	L-61u-0H	==	C,sH2sN3O,S.HC@ 120-123C decomp.	нсд 8	*1.33(3 2.26-2. (1H), 3. 4.61(1H), 12	*1.33(3H), 1.37(3H), 1.65-2.13(4H) 2.26-2.39(2H), 2.40-2.57(2H), 2.7 (1H), 3.46(3H), 3.88(1H), 4.23(1H) 4.61(1H), 8.14(1H), 8.41(2H), 8.48 (1H), 12.10(1H)	3H), 1.65 .40-2.57 .88(1H), H), 8.41(*1.33(3H), 1.37(3H), 1.65-2.13(4H), 2.26-2.39(2H), 2.40-2.57(2H), 2.79 (1H), 3.46(3H), 3.88(1H), 4.23(1H), 4.61(1H), 8.14(1H), 8.41(2H), 8.48 (1H), 12.10(1H)
F-26	- - - - - - - - - - - - -			L-Ser-OH	=	С.3H23N3O7S+HC@ 115-119°C decomp.	нсд 8	*1.40((211), 2.3.86(11), 8.	*1. 40(6H), 1. 88-2. 20(2H), 2. 26-2. (2H), 2. 79(1H), 3. 40(2H), 3. 58(3H) 3. 86(1H), 4. 25(1H), 4. 65(1H), 8. 11 (1H), 8. 20-8. 44(3H), 12. 65(1H)	2. 20(2H), .40(2H), H), 4. 65(3H), 12. 6	*1. 40(6H), 1. 88-2. 20(2H), 2. 26-2. 64 (2H), 2. 79(1H), 3. 40(2H), 3. 58(3H), 3. 86(1H), 4. 25(1H), 4. 65(1H), 8. 11 (1H), 8. 20-8. 44(3H), 12. 65(1H)
F - 27	II-F-01n-0II		<u> </u>	L-Pro-011	H	C, sH2 s N3 O 6 S · HC 2 137 - 142 ° - decomp	нсе 8	*1.33(3 2.30-2. 3.60-3. (111),8.	*1. 33(3H), 1. 38(3H), 1. 76-2. 24 2. 30-2. 60(2H), 2. 93(1H), 3. 50(3. 60-3. 95(3H), 4. 21-4. 30(1H), (1H), (1H), 8. 22-8. 62(3H), 12. 50(1H)	3H), 1.76 . 93(1H), . 21-4.30 3H), 12.5	*1. 33(3H), 1. 38(3H), 1. 76-2. 24(6H), 2. 30-2. 60(2H), 2. 93(1H), 3. 50(2H), 3. 60-3. 95(3H), 4. 21-4. 30(1H), 4. 92 (1H), 8. 22-8. 62(3H), 12. 50(1H)

55	50	45	40	35		30	25	20	15	10	5
Table	e 1 (contin	nued)									
F-28	JI0-n19-7-II			CH2COOI	=======================================	C2.1H29N3O9S-HC2 120-124T decomp.	<u>L</u>	8 8	**1. 26(6H), 2. 01-2. 19(2H), 2. 34- 2. 62(2H), 2. 80-2. 96(1H), 3. 12-3. 25 (1H), 3. 97(1H), 4. 32(1H), 4. 66(3H), 6. 85(2H), 7. 15(2H)	11-2. 19(2H 2. 96(1H), 4. 32(1H), 2H)), 2. 34- 3. 12-3. 25 4. 66(3H),
- 2 d	II - T - Q I n - O I		:	SO ₃ H DL-Phe-OH	=	C19H27N3O9S2. HC2 216-220°C decomp.		* 0 0 1 0	*1.32(6H), 1.86-2.03(2H), 2.24-2.40 (2H), 2.63(1H), 3.05-3.22(2H), 3.78 (4H), 3.96(1H), 4.46-4.61(2H), 7.15 -7.28(2H), 7.42-7.61(2H), 7.86(1H), 8.26-8.58(3H)	2. 03(2H), 3. 05-3. 22 4. 46-4. 61(-7. 61(2H),	2. 24-2. 40 (2H), 3. 78 (2H), 7. 15 7. 86(1H),
F-30	II-L .Asp-011			Gly-0H	=	C13H19N3O6S.HC2 146-149° decomp.	1	* 5	**1.39(3H), 1.45(3H), 2.94-3.21 (2H), 3.98(2H), 4.26(1H), 4.45(1H)	5(3H), 2. 94 4. 26(1H), 4	-3.21 .45(1H)
7- -31	H-L-Glu-0II		.i	НО	Ħ	C.oH.sN2OsS·HC2 52- 55T decomp.	•нс@ 8		**1.38(3H), 1.44(3H), 2.10-2.24 (2H), 2.53-2.62(2H), 4.01(1H), 4.43 (1H)	4(3H), 2. 10 (2H), 4. 01(-2. 24 1H), 4. 43
			-			1	-				_

**1.46(3H), 1.54(3H), 4.01(3H)		as respective
∞		
C7H14N2O3S·HCQ 57.5-59°C	decomb.	were isolated
==		32 4
G1y-0H		F-1 to F-3 and F-32 were des.
<u> </u>		t,
F-32 H		Compounds F-1 hydrochlorides.

Table 1 (continued)

 * ; measured in DMSO-d $_{6}$

 $\star\star$, measured in D_2O

Working Example 1 (Synthesis of the Compound 8)

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To the solution of $(N-\gamma-L-glutamyl-D-penicillamyl)glycine hydrochloride (F-5) (0.3 g) in 1N-hydrochloric acid (0.81 ml) and methanol (1.6 ml), was added dropwise at room temperature the solution of sodium nitrite (0.11 g) in water (0.5 ml). After stirring at room temperature for 30 minutes, methanol was evaporated off under reduced pressure, and the solid precipitated by addition of acetone to the residue which was washed with acetone, to give <math>(N-\gamma-L-glutamyl-S-nitroso-D-penicillamyl)glycine (0.19 g).$

Working Example 2 (Synthesis of the Compound 7)

To the solution of $(N-\gamma-L-glutamyi-D-penicillamyi)glycine hydrochloride (0.5 g) in methanol (5 ml), was added at 0 °C the solution of ethyl nitrite in ethanol (10%) (1.1 ml). At the same temperature a drop of 4N-hydrochloric acid-methanol solution was added, and the mixture was stirred for 30 minutes. The solvent was evaporated off under reduced pressure, and the resultant crystals were washed with diethyl ether, to give <math>(N-\gamma-L-glutamyl-S-nitroso-L-penicillamyl)glycine hydrochloride (0.5 g).$

In the same way, the Compounds 1 to 6, 9 to 11, and 13 to 34 listed in Table 2 shown below were synthesized.

Working Example 3 (Synthesis of the Compound 12)

To the solution of $(N-\beta-L-aspartyl-D-penicillamyl)glycine hydrochloride (0.2 g) in 1N-hydrochloric acid (0.56 ml) and water (1.0 ml), was added dropwise at room temperature the solution of sodium nitrite (0.077 g) in water (0.5 ml). The reaction mixture was stirred at room temperature for 30 minutes, loaded onto an LH-20 column, and eluted with water. The fractions containing the desired product were freeze-dfied, to give <math>(N-\beta-L-asparagyl-S-nitroso-D-penicillamyl)glycine (0.2 g).$

Table 2 shows the structure, physical properties, and NMR data of the Compounds 1 to 34 obtained in the Working Examples.

5	IR(KBr)(cm ⁻¹) others	3800-2350, 1735, 1681, 1550-1510, 1400, 1380, 1320, 1215, 1130, 1040, 1015, 660	3700-2200, 1733, 1655, 1515, 1395, 1375, 1220, 1126, 990, 663	3800-2200, 1735, 1650, 1515, 1395, 1375, 1220, 1128, 990, 665
15 20	NMR spectra	(3H), 4.02	1. 91(3H), 1. 94(3E), 1. 95 37 -2. 24(2H), 2. 34-2. 61 15 (2H), 3. 92(1H), 5. 19(1H) 11	1. 91(3H), 1. 94(3H), 2. 02 38 -2. 16(2H), 2. 40-2. 53 15 (2H), 3. 94(1H), 5. 17(1H) 11
25	NMR spread Ex. No. (8, pp	2 (2H), 4.81(1H)	2	62
30 !	Molecular formula Rephysical Reproperties E	C,H,3N3O,S.HCL	C.o.H., N.O.S. HC@ amorphous	С.,оН.,7 № 0.6 S. HC@ 68-75° decomp.
40	guration f Pen Y	G1y-0H	HO	IIO
≻ .	Configur X of 1	0	H-L-61u-0H	H-D-01u-0H
rable 2	punodwo	Ξ	2 II-L	3 H-D

	5 <i>0</i>	45	40	30 35		20	15	10	5
rable	le 2 (continu	nued)		. ;					
				Collis NoOsS		1.89(3H), 1	1.89(3H), 1.92(3H), 1.97	3700-2250, 1740, 1655	40, 1655,
-4.	ЯС		G1y-0H	amorphous	2	(3H), 3.87-3.98(2H),	3. 98(2Н),	1520, 1375, 1215, 1135,	15, 1135,
						5.16(1H)		1035, 665	
ļ	L	-		C, 2 H 2 0 N + 0 7 S • H C Q	0	1.88(3H), 1	1.88(3H), 1.98(3H), 1.90	3800-2150, 1738, 1650,	38, 1650,
iO	H-L-G1u-OH		Gly-0H	84-89°decomp.	2	-2. 22(2H), 2. 30-2. 67	2.30-2.67	1525, 1415, 1392, 1371,	392, 1371,
						(2H), 3.81-3.99(3H),	3.99(3H),	1215, 1130, 1035,	35, 665
						5.21(1H)			• ;
				C, 2 H 2 0 N + 0 7 S		1.90(3H), 1.99(3H), 1.	. 99(3H), 1. 90	3700-2400, 1640, 1520,	40, 1520,
9	H-L-61u-0II	<u> </u>	Gly-0H	amorphous		-2.13(2H), 2.26-2.65	2. 26-2. 65	1392, 1232	
						(2H), 3.67((2H), 3. 67(1H), 3. 77(2H)	UV(H ₂ O):λmax=	Įt.
		···-				5.21(1H)		;	340.0nm
				C, 2 H 2 0 N + 0 7 S - HCQ	10	1.89(3H), 1	1.89(3H), 1.98(3H), 1.90	3800-2200, 1738, 1650,	38, 1650,
_	H-L-Glu-011	 	G1y-0H	108-113°C	2	-2.16(2H), 2.40-2.56	2.40-2.56	1525, 1415, 1395,	95, 1371,
				decomp.		(2H), 3.91((2H), 3. 91(1H), 3. 93(2H)	1220, 1132, 1034,	134, 665
						5.20(1H)			
		·							

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e e	50	4 5	40	30 35		15 20 25	5
Tab	able 2 (contin	inued	1)				
	l			C.2H20N+07S+HC2		1.90(3H), 1.99(3H), 1.90	0 3800-2200, 1650, 1520,
∞	H-D-G1n-OH	<u> </u>	G1y-0H	100-105C	2	-2.17(2H), 2.36-2.60	1395, 1313, 1235, 1130,
				decomp.		(2H), 3. 91(1H), 3. 94(2H)) 665
						5.21(1H)	
		···		C12H20N+07S+HC0		1.91(3H), 2.01(3H), 2.00	0 3700-2300, 1720, 1660,
<u> </u>	H-L-61u-	<u>۔</u>	Gly-0H	38-1033	2	-2.24(2H), 2.30-2.60	1540, 1500, 1410, 1210,
		·		decomb.		(2H), 3. 95(2H), 4. 09(1H)	665
		<u>.</u> .				5.27(1H)	• •
	<u></u>	1		C, , H, 8 N, O 6 S		1.93(3H), 2.01(3H), 2.69	9 3700-2300, 1738, 1658,
10	H-L-Asp-OH	<u>_</u> .	G1y-0H	amorphous	8	-3.06(2H), 3.92-4.02	1526, 1385, 1218
		•				(3H), 5.24(1H)	UY(H ₂ O):\max=
							336. 8пш
	l			C.1H.8N3O6S.HC2		1.87(3H), 1.96(3H), 2.80	0 3700-2200, 1736, 1653,
=	H-L-Asp-OH	0	Gly-0H	95-100%	2	-3.09(2H), 3.80-4.04	1535, 1210, 665
				decomp.		(2H), 4. 27(1H), 5. 18(1H)	

	30, 1650,	0, 1370,	3, 665		5, 1650,	2, 1220,	10	• •		8, 1650,	0, 1220,				5, 1645,	0, 1225,	10		terror to the
	3700-2200, 173	1520, 1455, 139	1218, 1150, 83		3700-2250, 172	1520, 1394, 137	1145, 1128, 66			3700-2250, 173	1522, 1392, 137	1145, 868			3700-2200, 172	1520, 1390, 137	1210, 1150, 66		
	1), 2, 01	(H),	92(1H)	18(1H)), 1.89	80-	58(2H)	23(1H)), 1.90	95-	54	- 10	<u> </u>	46-	19	97(3H)	89(1H)	17(1H)
), 1. 91(31	90-2.17(2	55(2H), 3.	38(1H), 5.), 0.89(3H	38(3H), O.), 2. 37-2.), 4. 12-4.		, 0.91(3H	16(3H), 1.	, 2. 34-2.	0(1H), 4.	, 5.30(1H	2(6H), 1.	, 1. 79-2.	9(3H), 1.	0(2H), 3.	4. 25-4. 40(1H), 5. 17(1H)
	1.37(3H	(3H), 1.	2.39-2.	4.23-4.	0.86(3H)	(3H), 1.	2.23(3H)	3.91(1H)	5.25(1H)	0.87(3H)	(3H), 1.	2.23(3H)	(2H), 3. g	4.26(1H)	0.70-0.9	1.73(3H)	(2H), 1.8	2.35-2.6	4.25-4.4
		2				2		-			2					2			
	0,5.HC		·dwc		0,5·HC@		mp.			0,5.HC@		.dmc	·		D.S.HCd		-dwc		
	C13H22N+	107-1120	dec		CisH26N4	118-122°C	deco		İ	C15H26N4	112-117°C	deco			216 H 28 N + (120-1246	dec		
		L-31a-011				L-Val-OH													
nued						ــــ													- :
C1	l <u>.</u>	N-L-Glu-OH			L	H-L-Glu-0!				l	H-L-G1u-OH				1	H-L-G1u-011			
ab		~1				13				-	14					15			
	Table 2 (continued)	C1	2 (continued) -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.90-2.17(2H),	2 (continued) :- -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.90-2.17(2H), decomp.	2 (continued) :- -L-Giu-OH	2 (continued) -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.91(3H), 2.01 -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.90-2.17(2H), decomp. 4.23-4.38(1H), 5.18(1H) C.15HzeN+OrS·HC@ 0.86(3H), 0.89(3H), 1.89	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C -C.3H22N+O·S·HCg 2 (3H), 1.91(3H), 2.01 3700-2200, 1730, -L-Giu-OH L L-Ala-OH 107-112C 2 (3H), 1.90-2.17(2H), -C.39-2.55(2H), 3.92(1H), -C.5H26N+O·S·HCg 0.86(3H), 0.89(3H), 1.89 3700-2250, 1725, -L-Glu-OH 118-122C 2 (3H), 1.98(3H), 0.80- 1520, 1394, 1372,	2 (continued) -L-Glu-OH L L-Ala-OH 107-112C -L-Glu-OH L L-Val-OH 118-122C	2 (continued) -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.91(3H), 2.01 3700-2200, 1730, decomp. -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.90-2.17(2H), decomp. -L-Giu-OH L L-Ala-OH 118-122°C 2 (3H), 0.89(3H), 0.80- decomp. -L-Giu-OH L L-Val-OH 118-122°C 2 (3H), 1.98(3H), 0.80- decomp. -L-Giu-OH L L-Val-OH 118-122°C 2 (3H), 1.98(3H), 0.80- decomp. -L-Giu-OH L L-Val-OH 118-122°C 2 (3H), 1.98(3H), 1.98(3H), 1.89 3700-2250, 1725, decomp.	2 (continued) -L-Glu-OH L L-Ala-OH 107-112C C (3H), 1.90-2.17(2H), 1520, 1455, 1390, decomp. -L-Glu-OH L L-Val-OH 118-122C C (3H), 1.96(3H), 0.89(3H), 1.89 A 23-4.38(1H), 5.18(1H) -L-Glu-OH L L-Val-OH 118-122C C (3H), 1.98(3H), 0.80- 1520, 1394, 1372, decomp. 2 (3H), 1.98(3H), 0.80- 1520, 1394, 1372, decomp. 3.91(1H), 4.12-4.23(1H)	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C -L-Giu-OH L L-Val-OH 118-122C -L-Glu-OH L L-Val-OH 118-12C-0H 118-1360 -L-Glu-OH L L-Val-OH 118-12C-0H 118-1360 -L-Glu-OH L L-Val-OH 118-1360 -L-Glu-OH 118-1360 -L-Glu-O	2 (continued) -L-Giu-OH L L-Ala-OH 107-112°C 2 (3H), 1.91(3H), 2.01 3700-2200, 1730, -L-Giu-OH L L-Val-OH 118-12°C 2 (3H), 1.90-2.17(2H), 1520, 1455, 1390, -L-Glu-OH L L-Val-OH 118-12°C 2 (3H), 1.98(3H), 0.89(3H), 1.89 3700-2250, 1725, -L-Glu-OH L L-Val-OH 118-12°C 2 (3H), 1.98(3H), 0.80- 1520, 1394, 1372, -L-Glu-OH D L-Val-OH 112-117°C 2 (3H), 1.96(3H), 1.90 3700-2250, 1738, -L-Glu-OH D L-Val-OH 112-117°C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370,	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C -L-Giu-OH L L-Yal-OH 118-122C -L-Glu-OH L L-Yal-OH 112-117C -L-Glu-OH D L-Yal-OH 112-117C -L-Glu-OH	2 (continued) -L-Glu-OH L L-Ala-OH 107-112T -C.3H2.N.O.S·HC@ L.37(3H), I.91(3H), Z.01 3700-2200,1730, -L-Glu-OH L L-Ala-OH 107-112T C.3H2.L.SH2.N.O.S·HC@ L.38(1H), E.10(1H) 1218,1150, 835, -L-Glu-OH L L-Val-OH 118-122T C.5H2.N.O.S·HC@ 0.86(3H), 0.80- 1520,1328, 665 Gecomp. Z.23(3H), I.90(3H), I.90 3700-2250,1738, -L-Glu-OH D L-Val-OH 112-117T C.5H2.N.O.S·HC@ 0.87(3H), 0.91(3H), I.90 3700-2250,1738, -L-Glu-OH D L-Val-OH 112-117T Gecomp. Z.23(3H), I.95- 1522,1392,1370, -L-Glu-OH D L-Val-OH 112-117T C.5H2.N.O.S·HC@ 0.87(3H), 0.91(3H), I.95- 1522,1392,1370, -L-Glu-OH D L-Val-OH 112-117T C.5H2.N.O.S·HC@ 0.87(3H), 2.34-2.54 C.5H3.3.90(1H), 4.07-	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C (3H), 1.91(3H), 2.01 3700-2200,1730, decomp. 2.39-2.55(2H), 3.92(1H) 1218,1150, 835, 1390, decomp. 2.39-2.55(2H), 3.92(1H) 1218,1150, 835, 1390, decomp. 2.39-2.55(2H), 2.92(1H) 1218,1150, 835, 1390, decomp. 2.23(3H), 0.89(3H), 1.89 3700-2250,1725, decomp. 2.23(3H), 2.37-2.58(2H) 1145,1128, 665 3.91(1H), 4.12-4.23(1H) 5.25(1H) 5.25(1H) 5.25(1H) 12.117C 2.23(3H), 1.90 3700-2250,1738, decomp. 2.23(3H), 2.34-2.54 1145, 868 4.26(1H), 4.07- 4.26(1H), 5.30(1H), 4.07- 4.26(1H), 5.30(1H), 5.30(1H), 5.30(1H) 5.20(1H), 5.30(1H), 5.	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C 2 (3H), 1.91(3H), 2.01 3700-2200, 1730, decomp. -L-Giu-OH L L-Val-OH 118-12C 2 (3H), 1.96(3H), 0.89(3H), 1.89 3700-2250, 1725, 180H) -L-Glu-OH L L-Val-OH 118-12C 2 (3H), 1.98(3H), 0.80- 1520, 1394, 1372, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95- 1522, 1392, 1370, decomp. -L-Glu-OH D L-Val-OH 112-117C 3 (2H), 3.90(1H), 4.07- 4.26(1H), 5.30(1H)	2 (continued) -1-Glu-OH L L-Ala-OH 107-112C 2 (3H), 1.91(3H), 2.01 3700-2200, 1730, decomp. -1-Glu-OH L L-Ala-OH 107-112C 2 (3H), 1.91(3H), 2.01 1220, 1455, 1390, decomp. -1-Glu-OH L L-Val-OH 118-122C 2 (3H), 1.98(3H), 0.80 1520, 1394, 1372, decomp. -1-Glu-OH L L-Val-OH 118-122C 2 (3H), 1.96(3H), 0.80 1520, 1394, 1372, decomp. -1-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95 1522, 1392, 1370, decomp. -1-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95 1522, 1392, 1370, decomp. -1-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.96(3H), 1.95 1522, 1392, 1370, decomp. -1-Glu-OH L L-Leu-OH 120-124C 2 173(3H), 1.79-2.19 1520, 1390, 1370, decomp.	2 (continued) -L-Giu-OH L L-Ala-OH 107-112C 2 (3H), 1.90-2.17(2H), 1520, 1455, 1390, decomp. -L-Giu-OH L L-Val-OH 118-122C 2 (3H), 1.90-2.17(2H), 1518, 1150, 835, 1390, decomp. -L-Glu-OH D L-Val-OH 112-117C 2 (3H), 1.98(3H), 0.89-1720, 1128, 665 3.91(1H), 4.12-4.23(1H) 5.25(1H) 6.25(1H) 7.25(1H) 7.26(1H), 1.95-1139, 1370, 1320, 1330, 1370, decomp. 7.25(1H), 1.95-1139, 1370, decomp. 7.25(1H), 1.95(1H), 4.07-1145, 668 7.25(1H), 1.95-1197, 1390, 1370, decomp. 7.25(1H), 1.95(1H), 1.95-1197, 1390, 1370, decomp. 7.25(1H), 1.95(1H), 1.95-1197, 1390, 1370, decomp. 7.25(1H), 1.95(3H), 1.97(3H), 1.100, 1150, 665	2 (continued) -L-Giu-OH L L-Aia-OH 107-112C 2 (3H), L.90-2.17(2H), 1520, 1455, 1390, decomp. -L-Giu-OH L L-Aia-OH 107-112C 2 (3H), L.90-2.17(2H), 1218, 1150, 835, 1390, decomp. -L-Giu-OH L L-Val-OH 118-122C 2 (3H), L.98(3H), 0.80- 1520, 1394, 1372, decomp. -L-Giu-OH D L-Val-OH 112-117C 2 (3H), L.96(3H), L.96-200, 1738, decomp. -L-Giu-OH D L-Val-OH 112-117C 2 (3H), L.96(3H), L.96-200, 1738, decomp. -L-Giu-OH L L-Leu-OH 120-124C 2 (2H), S.30(1H) 3 700-2250, 1738, decomp. -L-Giu-OH L L-Leu-OH 120-124C 2 (2H), 1.89(3H), L.97-219 3 700-2200, 1725, decomp. -L-Giu-OH L L-Leu-OH 120-124C 2 (2H), L.96(3H), L.97-319 1210, 1150, 665 2 (2H), L.91-38(3H), L.97-319 1210, 1150, 665

55		50	45	4 0	35	30	25	20	15	10	5	
TaJ	ab.	ble 2 (continu	ued)		· •							1
L			 		C, sH2+N+0,S+HC@	S-HCØ	<u>-</u>	1.87(3H), 2.02(3H), 1.64	3H), 1.64	3650-2200, 1740, 1625,	1740, 1623	ις.
	91	H-L-G1u-OH	<u></u>	L-Pro-0H	120-125T	2	-2	-2.52(8H), 3.68-3.93	-3.93	1505, 1450, 1210, 1190,	1210, 1190	0
					decomb.	. di	(3	(3H), 3.86(1H), 5.56(1H)	5. 56(1H)	665		
									,			
_		1_			C. BHzeN+O,S.HCQ	S-HC@	ļ-i	1.74(3H), 1.87(3H), 1.90	3H), 1.90	3800-2200, 1730, 1650,	1730, 1650	0
	17	H-L-G1u-OH	د	L-Phe-OH	122-127C	2	-2	-2.19(2H), 2.21-2.50	-2.50	1520, 1459, 139	1395, 1374,	- 4.
					decomp	•đu	(2	(2H), 2. 75-2. 98(1H),	(1H),	1225, 1132,	703:	-
							رى دى	3.08-3.28(1H), 3.89(1H)	3.89(1H)			
							4.	55-4.70(1H), 5.10(1H)	5.10(1H)			
						-	7.	7.06-7.40(5H)				
1		1			C H 2 6 N + O 8 S · HCQ	S-HC@	_ <u></u>	1. 76(3H), 1.86(3H), 1.94	3H), 1.94	3800-2200, 1730, 1650,	1730, 1650	0,
	8	H-L-G1u-011		1,-Tyr-OH	107-1120		-2	-2.14(2H), 2.20-2.46	-2.46	1518, 1450, 1395,	137	ເດົ
					decomp	·đ	(2	(2H), 2.77(1H), 3.15(1H)	3.15(1H)	1230, 1130, 1110,	1110, 835,	Š
						No.	<u>ښ</u>	3.87(1H), 4.55-4.70(1H)	4.70(1H)	670		
						-	٠٠.	5.08(1H), 6.70(2H),	2H),			
		· -					7.	7.03(1H)				

5	1730, 1655, 1395, 1375, 665	40, 1650, 93, 1372, 32, 702	735, 1650,	5, 1650, 0
10	3800-2230, 1520, 1455, 1220, 1135,	3700-2150, 1740, 1520, 1458, 1393, 1232, 1125, 1032,	3700-2200, 173 1525, 1225, 63	3700-2200, 1735, 1650, 1520, 1225, 670
15	1.70	(1H) 6.18),	2 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	(3H) 2. 1),
20	1.88(3H), 1.97(3H), 1.70 -2.50(8H), 3.90(1H), 4.39(1H), 5.17(1H)	*1.91(3H), 1.96(3H), 2.20-2.57(4H), 3.40(1H) 3.82(1H), 5.46(1H), 6.18 (1H), 7.18-7.40(10H), 8.40(3H), 8.62(1H), 9.51 (1H)	1. 92(3H), 2. 00(3H), 2. 92 -2. 19(2H), 2. 42-2. 55 (2H), 2. 86-2. 96(2H), 3. 93(1H), 4. 72(1H), 5. 20 (1H)	1.82-2.26(4H), 1.92(3H), 2.01(3H), 2.03(3H), 2.37-2.66(4H), 3.95(1H), 4.54(1H), 5.20(1H)
	2 4 4	8 (3 5 *)		1. 37.
30			100	CQ 2
35	C.sH2+N+OsS.HC@ 80-85Cdecomp.	СгэНгв N+ О5 S·НС <u>Ø</u> 120-130°C decomp.	C.,H.2.N.O.S.HC@ 84-88°C decomp.	C.5H25N4O7S.HC@ 104-109° decomp.
40	П-01п-0Н	NHCHPh ₂	HO - d s F	L-Met-0H]
45 an r.				
00 COnti	I-L-Glu-0H	H-L-61u-0II	H-F-010-7-H	H-L-Glu-OH
9 1 2 55	6.	20	21	22

5	3700-2200, 1730, 1650, 1520, 1220, 670	3700-2200, 1735, 1645, 1520, 1230, 700 ⁻³	3700-2200, 1730, 1645, 1520, 1390, 1370, 1225, 665
15),), 1(3H) 1(3H)	91 6- 7(1H) 3.81 7(1H) 9(1H)	5- 1.96),
20	0.82(3H), 0.88(3H), 1.22 (1H), 1.27-1.53(1H), 1.77-2.24(3H), 1.91(3H), 1.99(3H), 2.41-2.53 (2H), 3.94(1H), 4.24 (1H), 5.25(1H)	*1.80-2.20(2H), 1.91 (3H), 1.96(3H), 2.26- 2.44(2H), 3.60(1H), 3.81 (1H), 5.45(1H), 6.17(1H), 7.20-7.43(10H), 8.32 (3H), 8.56(1H).9.49(1H)	0. 75-1. 01(6H), 1. 45- 1. 76(3H), 1. 92(3H), 1. 96 (3H), 2. 06-2. 20(2H), 2. 43-2. 61(2H), 3. 95(1H) 4. 30(1H), 5. 27(1H)
25	0.82(3F (1H), 1. 1.77-2. 1.99(3 (2H), 3. (1H), 5.	*1.80 (3H), 2.44((1H), ,7.20 (3H),	0.75- 1.76((3H), 2.43- ,4.30
	2	7	~
30	.HC2	Э . • .	нСб
35	С.6Н28N+0,S·НС@ 109-115°C десомр.	C23H28N+05S.HC2 150-1557 decomp.	C,6H28N+07S-HC@ 130-136T decomp.
40	- 1 e - 0 7	NHCH Ph.	H0-nen-0H
реп 45		<u></u>	Δ
s ble 2 (contir	H-L-Glu-0H	H-L-Glu OH	H-L-Glu-OH
ධ අ E	2	त्त ८७	25

55	50	45	40	35		20	15	10	
Table	e 2 (cont.	inued	7)						
	<u></u>			C13H25N+07S+HCQ	0	1.63(6H), 1.89-2.25		3700-2200, 1730, 1650,	1650,
56	H-L-Glu-OH	0	L-Phe-OH	120-125℃	2	(2H), 2. 30-2. 66(2H),		1520, 1455, 1390, 1370,	1370,
				decomp.		2.94(1H), 3.18-3.43		1220, 1125, 700,	665
						(1H), 3.91(1H), 4.63-			
		-				4.70(1H), 5.12(1H),			
						7.05-7.50(5H)			
	1			C15H2+N+O9S+HC2	2	0.80-2.27(4H), 1.92		3700-2200, 1730, 1	1650,
27	H-L-Glu-OH		L-Glu-0H	91- 96°C	2	(3H), 1.97(3H), 2.34-	1	1520, 1220, 6655	
				decomp.		2.64(4H), 3.95(1H),			
						4.34(1H), 5.25(1H)			
	i			C13H23N4O8S.HCQ		1.94(3H), 2.03(3H),		3800-2200, 1735, 1	1650,
23	H-L-61u-0H	_:	1Ser-OH	89-92~	2	2.05-2.22(2H), 2.42-		1520, 1390, 1370, 122	225,
				decomb.		2.55(2H), 3.79-4.02		1135, 1070, 665	
						(3H), 4. 52(1H), 5. 29(1H)	(1H)		
	i			C, sH2+N40,S.HC0		1.87(3H), 1.90-2.36		3700-2200, 1735, 1	1630,
5.9	H-L-Glu-OH	Ω	L-Pro-OH	77-81°C	2	(6H), 2.01(3H), 2.43-		1510, 1450, 1220, 1190,	190,
	***			decomb.		2.57(2H), 3.68-3.89		665	
						(2H), 3.96(1H), 4.32			
,			:	•	1	(1H), 5.64(1H)			

	1650,	670						1655,	1120,						1655,	1210,	
5	3700-2200, 1735, 1650,	835,						1735;	1520, 1215, 1180, 1120,	680					1740,	1390,	
10	-2200,	1515, 1220,						.2200,	1215,	1035, 1005,					2200,	1410,	660
	3700-	1515,						3700-2200, 1735; 1655,	1520,	1035,					3750-2200, 1740, 1655,	1535, 1410, 1390, 1210,	1130,
15	1.96	4.3			•	6.82		1.95	13		~		~	_	2.87		
	1.77(3H), 1.87(3H), 1.	-2.12(2H), 2.31-2.43	(2H), 2.76-2.92(1H),	3.10-3.26(1H), 3.90	(1H), 4.51-4.70(1H),	4.64(2H), 5.11(1H), 6.82	\sim	1.79(3H), 1.89(3H), 1.95	-2. 21(2H), 2. 31-2. 43	(2H), 2.82-2.97(1H),	3.06-3.19(1H), 3.93	(1H), 4. 52-4. 73(1H),	5.13(1H), 7.28-7.43	(2H), 7.59-7.78(2H)	1.91(3H), 2.00(3H), 2.87	-3.14(2H), 3.97(2H),	1(1H)
20), 1.8	H), 2.	76-2.	26(1H	51-4.), 5. 1	13(2H)), 1.8	H), 2.	82-2.	19(1H)	52-4.), 7.28	59-7.), 2. 0(H), 3.), 5. 2
0.5	77(3H	. 12(2	H), 2.	10 - 3.	H), 4.	64 (2H)	(2H), 7.13(2H)	79(3H)	21(2)	H), 2.	06-3.	H), 4.	13(1H)	I), 7.	91(3H)	14(21	4.24(1H), 5.24(1H)
25	_ <u>-</u> -	-2	(2)	∾;	= 	₹:	(2)	<u> </u>	-2.	(2)		Ξ	ഹ	(21	i	ر اع	4.
		۲۵							2							2	
30	.S.			•				.250			•				S-HC@		•
1	10+N 8	8	121	decomb.				6 N 4 O 1	8	45t	decomb				8 N 4 O 7	្ហា06	decomp.
35	C21H28N+010S-	HCQ	108-1120	ģ				C19H26N4O10S2.	HCQ	140-145°	de				C H. 8 N. 0, S. HC@	85- 90°	ф
40	l	-0H						SO ₂ H	e-0H				·			#10-	
	CH COOH	L-Tyr-OH						80	DL-Phe-OH							Gly-0H	
(pənu															-		
contin		n-01							HO-n.							110-ds4-	
50 2	. –	-[61						1	H-L-61							-1-4s	
able		± 0						 							-	===	
55 H		3							31							32	
-5																	

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	3800-2200, 1735, 1650 1520, 1210, 1115, 660	3800-2200, 1735, 1680, 1540, 1505, 1400, 1315, 1200, 655
	1. 93(3H), 1. 96(3H), 2. 06 3800-2200, 1735, 1650, -2. 18(2H), 2. 44-2. 55 1520, 1210, 1115, 660 (2H), 3. 98(1H), 5. 19(1H)	1.95(3H), 2.12(3H), 4.05 3800-2200, 1735, 1680, (2H), 4.83(1H) 1540, 1505, 1400, 1315, 1200, 655
	2	2
	C.oH.rN3O8S·HC@ 73-80℃ decomp.	C7H13N3O+S.HCQ 63-68C decomp.
uea)	110	НО- 419
Table 2 (continue	H-L-G1u-OH	=
Tabl	 3	34

isolated 34 were 9, and 11 3, 5, 7 -Compounds $l \sim 3$, $\tilde{\imath}$, $\tilde{\imath}$ - respective hydrochlorides.

the . ೮ \star ; measured by using DMSO-d $_6$ as the solvent and TMS internal standard. Preparation Examples

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Preparation Example 1		
(1) Compound 1 (2) lactose (3) corn starch (4) magnesium stearate	2 g 196 g 50 g 2 g	

(1), (2) and 20 g of corn starch were mixed and granulated together with a paste made from 15 g of corn starch, to which 15 g of cornstarch and (4) were added. The mixture was compressed with a compress-tableting machine, to produce 2000 tablets of 3 mm in diameter containing 1 mg of (1) in each tablet.

Preparation Example 2			
(1) Compound 2	4 g		
(2) lactose	194 g		
(3) corn starch	40 g		
(4) magnesium stearate	2 g		

(1), (2) and 15 g of corn starch were mixed and granulated together with a paste made from 15 g of corn starch, to which 10 g of corn starch and (4) were added. The mixture was compressed with a compress-tableting machine, to produce 2000 tablets of 5 mm in diameter containing 2 mg of (1) in each tablet.

Preparation Example 3		
(1) Compound 1(2) Avicel (crystalline cellulose)(3) lactose(4) magnesium stearate	100 mg 300 mg 595 mg 5 mg	

(1), (2), (3) and (4) described above were mixed thoroughly, and compressed directly with a compress-tableting machine, to produce 100 sublingual tablets (3 mm in diameter) containing 1 mg of (1) in each tablet.

Experimental Example 1

In a 20 ml-tank (37°C, aerated with 95% O₂ + 5% CO₂, pH7.4), a specimen (pig left coronary descending artery (LAD), or rat aorta) was suspended. The specimen was allowed to contract by addition of PGF_{2a} (6 µM) for pig coronary artery or KCl (60 mM) or TEA (45 mM) + Ba (0.3 mM) for rat aorta, and then a test compound was added at a time or cumulatively; the relaxing effect of the compound on the constrictive tension was examined; the Compounds 1 and 2 showed a powerful relaxing effect.

Experiment Example 2

Relaxing effects on KC1 induced contraction in isolated rat aorta

Ring preparations of rat thoracic aorta were placed in $20m \, \mathrm{t}$ organ baths containing Krebs-Hemseleit solution kept at $37\,^{\circ}$ C, a pH of 7.4 and gassed with 95% $\mathrm{CO_2}$ - 5% $\mathrm{O_2}$. After steady state contraction induced by 60mM KC1, vasorelaxing effects of test compounds (10^{-6} , 10^{-7} mol/i) were examined. The vasorelaxing effects were expressed as % relaxation from the maximum contraction induced by 60mM KC1. The relaxing effects are shown in Table 3.

Table 3

Compound	10 ⁻⁷ M	Retension time/min	10 ⁻⁶ M	Retension time/min
2	18	24	62	>30
3	19	17	50	>30
5	16	25	47	>30
7	11	>30	64	>30
11	12	20	37	>30
13	19	>30	85	>30
14	11	12	74	>30
17	20	17	66	>30
19	19	20	58	>30
24	26	>30	75	>30

Claims

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1. A compound of the formula:

$$X_1 - \frac{X_3}{N} > CH - \frac{C}{C} - SNO$$

wherein R^1 and R^2 are independently a hydrogen atom or a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is a hydrogen atom, an acyl group, a lower alkoxy group or a hydrocarbon residue which may be substituted; X^2 is an acyl group or a carboxyl group which may be esterified or which may form an amide; with a proviso that when X^2 is a carboxyl group X^1 is not a hydrogen atom or acetyl group and that when both R^1 and R^2 are hydrogen atoms X^1 is not an acetyl group or γ -glutamyl group, or a salt thereof.

2. A compound according to claim 1, wherein R^1 and R^2 are independently a hydrocarbon residue which may be substituted, or R^1 and R^2 may be bound to each other to form a ring of the formula: - $(CH_2)_n$ -wherein n is an integer of 2 to 6.

- 3. A compound according to claim 1, wherein X1 is an amino acid derived acyl.
- 4. A compound according to claim 1, wherein R^1 and R^2 are independently a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is an amino acid derived acyl; X^2 is an acyl group or a carboxyl group which may be esterified or which may form an amide.
- 5. A compound according to claim 1, wherein the hydrocarbon residue represented by R¹, R², R³ or X¹ is a chain saturated, chain unsaturated, cyclic saturated or cyclic unsaturated hydrocarbon residue, each of which may be substituted by one to three groups selected from the class consisting of halogen atom, nitro, nitrile, hydroxyl, carboxyl, C¹-4 alkoxy, C¹-4 alkylthio, amino, mono- or di-C¹-4 alkyl amino, mono- or di-aralkylamino, mono- or di-pyridylamino, C¹-4 alkoxycarbonyl, cyclo C³-6 alkylcarbonyl, carbamoyl, mono- or di-C¹-4 alkylcarbamoyl, and phenyl, phenoxy, benzoyl, phenoxycarbonyl, phenyl C¹-4 alkylcarbamoyl or

phenylcarbamoyl group, in which each of said phenyl group may be substituted by 1 to 4 groups selected from the class consisting of C_{1-4} alkyl, halogen atom, hydroxyl, benzyloxy, amino, mono- or di- C_{1-4} alkylamino, niro and C_{1-4} alkoxycarbonyl.

- 6. A compound according to claim 1, wherein the acyl group represented by R^3 , X^1 or X^2 is a carboxylic, carbamic, sulfonic or oxycarboxylic acyl group, each of which may be substituted by one to three groups selected from the class consisting of halogen atom, nitro, nitrile, hydroxyl, carboxyl, C_{1-4} alkoxy, C_{1-4} alkylthio, amino, mono- or di- C_{1-4} alkyl amino, mono- or di-aralkylamino, mono- or di-pyridylcarbonylamino, C_{1-6} alkylcarbonyl, C_{1-4} alkoxycarbonyl, cyclo C_{3-6} alkylcarbonyl, carbamoyl, mono- or di- C_{1-4} alkylcarbamoyl group, in which each of said phenyl may be substituted by 1 to 4 groups selected from the class consisting of C_{1-4} alkyl, halogen atom, hydroxyl, benzyloxy, amino, mono- or di- C_{1-4} alkylamino nitro and C_{1-4} alkoxycarbonyl.
- 7. A compound according to claim 1, wherein the lower alkoxy group is C_{1-6} alkoxy group.
- 8. A compound according to claim 1, wherein the carboxyl group which may be esterified is carboxyl or a group of the formula: -CO-OR⁵
 - wherein R⁵ is a hydrocarbon residue which may be substituted.

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9. A compound according to claim 1, wherein the carboxyl group which may form an amide is carboxyl or a group of the formula:

$$-CO-N/R^{\sigma}$$

- wherein R⁶ is a hydrogen atom or a hydrocarbon residue which may be substituted, and R⁷ is a hydrogen atom or a lower alkyl group or R⁶ and R⁷ may form a cyclic amino group together with the adjacent nitrogen atom.
 - 10. \bar{A} compound according to Claim 1, wherein R^1 and R^2 are independently a chain saturated or cyclic unsaturated hydrocarbon residue, or R^1 and R^2 together with the adjacent carbon atom form cyclopentyl or cyclohexyl.
 - 11. A compound according to claim 1, wherein R^1 and R^2 are independently $C_{1-\epsilon}$ alkyl group.
 - 12. A compound according to claim 1, wherein R¹ and R² are methyl.
 - 13. A compound according to claim 1, wherein R3 is a hydrogen atom or an acyl group.
 - 14. A compound according to claim 13, wherein the acyl group is C_{1-6} alkyl carbonyl or C_{6-10} aryl carbonyl.
 - 15. A compound according to claim 1, wherein R3 is a hydrogen atom.
 - 16. A compound according to claim 1, wherein X1 is a hydrogen atom or an acyl group.
 - 17. A compound according to claim 16, wherein the acyl group is an amino acid derived acyl group.
 - 18. A compound according to claim 17, wherein the amino acid is glycine, alanine, glutamic acid, leucine, isoleucine, phenylalanine, aspartic acid, cysteine, sarcosine, glutamine, asparagine or proline.
- 19. A compound according to claim 17, wherein the amino acid is glycine, aspartic acid, asparagine, glutamic acid, glutamine or phenylalanine.
- 20. A compound according to claim 17, wherein the amino acid is glutamic acid or aspartic acid.
- 21. A compound according to claim 1, wherein X2 is a carboxyl group which may be esterified.
- 22. A compound according to claim 1, wherein X² is a carboxyl or carbamic acyl group.
- 23. A compound according to claim 22, wherein the carbamic acyl group is carbonyl amino or a carboxyl group forming an amide with an amino acid.
- 24. A compound according to claim 23, wherein the amino acid is glycine, alanine, glutamic acid, leucine, isoleucine, phenylalanine, aspartic acid, cysteine, sarcosine, glutamine, asparagine or proline.
- 25. A compound according to claim 23, wherein the amino acid is glycine, aspartic acid, asparagine, phenylalanine, glutamic acid or glutamine.
 - 26. A compound according to claim 1, wherein R^1 and R^2 are independently C_{1-6} alkyl, phenyl or naphthyl, or R^1 and R^2 form cyclopentyl or cyclohexyl together with the adjacent carbon atom; R^3 is a hydrogen atom or a C_{6-10} aromatic acyl group; X^1 is a hydrogen atom or an amino acid derived acyl group in which said amino acid is selected from the group consisting of glycine, aspartic acid, phenylalanine, asparagine, glutamic acid and glutamine; X^2 is a carboxyl group, carbonylamino or a carboxyl group forming an amide with an amino acid residue in which said amino acid is selected from the group consisting of glycine, aspartic acid, phenylalanine, asparagine, glutamic acid and glutamine.

- 27. A compound according to claim 1, wherein the salt is a pharmaceutically acceptable salt.
- 28. A compound according to claim 1, which is N-(N-L-y-Glutamyl-D-penicillamyl)glycine.
- 29. A compound according to claim 1, which is N-(N-L-γ-Glutamyl-L-penicillamyl)-L-valine.
- 30. A compound according to claim 1, which is N-(N-L-γ-Glutamyl-L-penicillamyl)-L-phenylalanine.
- 31. A compound according to claim 1, which is N-(N-L-y-Glutamyl-L-penicillamyl)-L-glutamic acid.
- 32. A compound according to claim 1, which is N-(N-L-y-Glutamyl-D-penicillamyl)diphenylmethylamine.
- 33. A pharmaceutical composition suitable for the therapy or prophylaxls of hypertension or angina pectoris which comprises (a) as the active ingredient, an effective amount of a compound according to claim 1 or a salt thereof and (b) a pharmaceutically acceptable carrier, excipient or diluent therefor.
- 34. The use of a compound according to claim 1 or a salt thereof for the preparation of a medicine for the therapeutic treatment of a mammal.
 - 35. A method for producing a compound of the formula

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$$X' - \frac{N}{N} > CH - \frac{K}{C} - SNO$$

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wherein R^1 and R^2 are independently a hydrogen atom or a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is a hydrogen atom, an acyl group, a lower alkoxy group or a hydrocarbon residue which may be substituted; X^2 is an acyl group or a carboxyl group which may be esterified or which may form an amide; with a proviso that when X^2 is a carboxyl group X^1 is not a hydrogen atom or acetyl group and that when both R^1 and R^2 are hydrogen atoms X^1 is not acetyl group or γ -glutamyl group, or a salt thereof, which comprises.

(a) subjecting a compound of the formula (II):

$$X^{1} - \frac{R^{3}}{N^{2}} > CH - \frac{R^{1}}{C} - SH$$

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wherein R¹, R², R³, X¹ and X² are the same as described above to the nitrosation reaction, and, if desired,

(b) converting a product obtained by the above process (a) into a salt thereof.

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Claims for the following Contracting State: ES

1. A method for producing a compound of the formula (I):

$$X_1 - \frac{X_2}{K_2} > CH - \frac{K_2}{K_2} = SHO$$

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wherein R^1 and R^2 are independently a hydrogen atom or a hydrocarbon residue which may be substituted; R^3 is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X^1 is a hydrogen atom, an acyl group, a lower alkoxy group or a hydrocarbon residue which may be substituted; X^2 is an acyl group or a carboxyl group which may be esterified or which may form an amide; with a proviso that when X^2 is a carboxyl group X^1 is not a hydrogen atom or acetyl group and that when both R^1 and R^2 are hydrogen atoms X^1 is not acetyl group or -glutamyl group, or a salt thereof, which comprises.

(a) subjecting a compound of the formula (II):

$$\begin{array}{c} X^{1} - \overset{R^{3}}{\underset{X^{2}}{|}} > CH - \overset{R^{1}}{\underset{R^{2}}{|}} > SH \end{array}$$

wherein R^1 , R^2 , R^3 , X^1 and X^2 are the same as described above to the nitrosation reaction, and, if desired.

(b) converting a product obtained by the above process (a) into a salt thereof.

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2. A method according to claim 1, wherein R^1 and R^2 are independently a hydrocarbon residue which may be substituted, or R^1 and R^2 may be bound to each other to form a ring of the formula: $-(CH_2)_0$ - wherein n is an integer of 2 to 6.

3. A method according to claim 1, wherein X1 is an amino acid derived acyl.

4. A method according to claim 1, wherein R¹ and R² are independently a hydrocarbon residue which may be substituted; R³ is a hydrogen atom, an acyl group or a hydrocarbon residue which may be substituted; X¹ is an amino acid derived acyl; X² is an acyl group or a carboxyl group which may be esterified or which may form an amide.

5. A method according to claim 1, wherein the hydrocarbon residue represented by R^1 , R^2 , R^3 or X^1 is a chain saturated, chain unsaturated, cyclic saturated or cyclic unsaturated hydrocarbon residue, each of which may be substituted by one to three groups selected from the class consisting of halogen atom, nitro, nitrile, hydroxyl, carboxyl, C_{1-4} alkoxy, C_{1-4} alkylthio, amino, mono- or di- C_{1-4} alkyl amino, mono- or di-pyridylamino, C_{1-4} alkoxycarbonyl, cyclo C_{3-6} alkylcarbonyl, carbamoyl, mono- or di- C_{1-4} alkylcarbamoyl, and phenyl, phenoxy, benzoyl, phenoxycarbonyl, phenyl C_{1-4} alkylcarbamoyl or phenylcarbamoyl group, in which each of said phenyl group may be substituted by 1 to 4 groups selected from the class consisting of C_{1-4} alkyl, halogen atom, hydroxyl, benzyloxy, amino, mono- or di- C_{1-4} alkylamino, niro and C_{1-4} alkoxycarbonyl.

6. A method according to claim 1, wherein the acyl group represented by R³, X¹ or X² is a carboxylic, carbamic, sulfonic or oxycarboxylic acyl group, each of which may be substituted by one to three groups selected from the class consisting of halogen atom, nitro, nitrile, hydroxyl, carboxyl, C¹-4 alkoxyl, C¹-4 alkylthio, amino, mono- or di-C¹-4 alkyl amino, mono- or di-aralkylamino, mono- or di-pyridylcarbonylamino, C¹-6 alkylcarbonyl, C¹-4 alkoxycarbonyl, cyclo C³-6 alkylcarbonyl, carbamoyl, mono- or di-C¹-4 alkylcarbomyl, and phenyl, phenoxy, benzoyl, phenoxycarbonyl, phenyl C¹-4 alkylcarbamoyl or phenylcarbamoyl group, in which each of said phenyl groups may be substituted by 1 to 4 groups selected from the class consisting of C¹-4 alkyl, halogen atom, hydroxyl, benzyloxy, amino, mono- or di-C¹-4 alkylamino nitro and C¹-4 alkoxycarbonyl.

7. A method according to claim 1, wherein the lower alkoxy group is C_{1-6} alkoyl group.

8. A method according to claim 1, wherein the carboxyl group which may be esterified is carboxyl or a group of the formula: -CO-OR⁵

wherein R5 is a hydrocarbon residue which may be substituted.

9. A method according to claim 1, wherein the carboxyl group which may form an amide is carboxyl or a group of the formula:

$$-CO-N/R^6$$

wherein R⁶ is a hydrogen atom or a hydrocarbon residue which may be substituted, and R⁷ is a hydrogen atom or a lower alkyl group or R⁶ and R⁷ may form a cyclic amino group together with the adjacent nitrogen atom.

10. A method according to claim 1, wherein R¹ and R² are independently a chain saturated or cyclic unsaturated hydrocarbon residue, or R¹ and R² together with the adjacent carbon atom form cyclopentyl or cyclohexyl.

11. A method according to claim 1, wherein R¹ and R² are independently C1-6 alkyl group.

12. A method according to claim 1, wherein R¹ and R² are methyl.

13. A method according to claim 1, wherein R3 is a hydrogen atom or an acyl group.

- 14. A method according to claim 13, wherein the acyl group is C₁₋₆ alkyl carbonyl or C₁₋₁₀ aryl carbonyl.
- 15. A method according to claim 1, wherein R3 is a hydrogen atom.
- 16. A method according to claim 1, wherein X1 is a hydrogen atom or an acyl group.
- 17. A method according to claim 16, wherein the acyl group is an amino acid derived acyl group.
- 18. A method according to claim 17, wherein the amino acid is glycine, alanine, glutamic acid, leucine, isoleucine, phenylalanine, aspartic acid, cysteine, sarcosine, glutamine, asparagine or proline.
 - 19. A method according to claim 17, wherein the amino acid is glycine, aspartic acid, asparagine, glutamic acid, glutamine or phenylalanine.
 - 20. A method according to claim 17, wherein the amino acid is glutarnic acid or aspartic acid.
- 21. A method according to claim 1, wherein X2 is a carboxyl group which may be esterified.
- 22. A method according to claim 1, wherein X2 is a carboxyl or carbamic acyl group.
- 23. A method according to claim 22, wherein the carbamic acyl group is carbonyl amino or a carboxyl group forming an amide with an amino acid.
- 24. A method according to claim 23, wherein the amino acid is glycine, alanine, glutamic acid, leucine, isoleucine, phenylalanine, aspartic acid, cysteine, sarcosine, glutamine, asparagine or proline.
 - 25. A method according to claim 23, wherein the amino acid is glycine, aspartic acid, asparagine, pheylalanine, glutamic acid or glutamine.
 - 26. A method according to claim 1, wherein R^1 and R^2 are independently C_{1-6} alkyl, phenyl or naphthyl, or R^1 and R^2 form cyclopentyl or cyclohexyl together with the adjacent carbon atom; R^3 is a hydrogen atom or
- a C₆₋₁₀ aromatic acyl group; X¹ is a hydrogen atom or an amino acid derived acyl group in which said amino acid is selected from the group consisting of glycine, aspartic acid, phenylalanine, asparagine, glutamic acid and glutamine; X² is a carboxyl group, carbonylamino or a carboxyl group forming an amide with an amino acid residue in which said amino acid is selected from the group consisting of glycine, aspartic acid, phenylalanine, asparagine, glutamic acid and glutamine.
- 25 27. A method according to claim 1, wherein the salt is a pharmaceutically acceptable salt.
 - 28. A method according to claim 1, wherein said compound (I) is N-(N-L-γ-GlutamyI-D-penicillamyI)glycine.
 - 29. A method according to claim 1, wherein said compound (I) is N-(N-L-y-GlutamyI-L-penicillamyI)-L-valine.
 - 30. A method according to claim 1, wherein said compound (I) is N-(N-L-γ-Glutamyl-L-penicillarnyl)-L-phenylalanine.
- 30 31. A method of a compound according to claim 1, wherein said compound (I) is N-(N-L-γ-Glutamyl-L-penicillamyl)-L-glutamic acid.
 - 32. A method according to claim 1, wherein siad compound (I) is N-(N-L- γ -Glutamyl-D-penicillamyl)-diphenylmethylamine.
- 33. A pharmaceutical composition for use in preparation of a medicine suitable for the therapy or prophylaxis of hypertension or angina pectoris which comprises (a) as the active ingredient, an effective amount of a compound as defined in claim 1 or a salt thereof and (b) a pharmaceutically acceptable carrier, excipient or diluent therefor.
 - 34. The use of a compound as defined in claim 1 or a salt thereof for the preparation of a medicine for the therapeutic treatment of a mammal.

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